Uniwersytet Warszawski

Wydział Psychologii

Syndrom poznawczo-uwagowy.

Korelaty neuronalne i związki z objawami psychopatologicznymi

Cognitive-attentional syndrome.

Neural correlates and relationships with psychopathology symptoms

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Streszczenie

Syndrom poznawczo-uwagowy (CAS) to kluczowy konstrukt w metapoznawczym modelu psychopatologii i psychoterapii. Składają się na niego nieadaptacyjne wzorce powtarzającego się negatywnego myślenia i dysfunkcjonalne przekonania metapoznawcze. W tym podejściu teoretycznym jest on konstruktem transdiagnostycznym, leżącym u podłoża różnego rodzaju zaburzeń psychicznych.

W poniższej pracy przedstawione zostały dwa artykuły naukowe. Głównym celem było potwierdzenie transdiagnostycznego statusu syndromu poznawczo-uwagowego. Pierwsza praca dotyczyła eksploracji związków nasilenia objawów CASu z objawami psychopatologicznymi i zaburzeniami psychicznymi. Druga objęła eksplorację różnic w funkcjonowaniu neuronalnym między osobami z wysokim i niskim nasileniem objawów CASu za pomocą indukcji ruminacji i pomiaru aktywności spoczynkowej mózgu podczas funkcjonalnego rezonansu magnetycznego.

Nasilenie objawów CASu jest powiązane z wyższym nasileniem różnych rodzajów objawów psychopatologicznych oraz jest związane z kilkukrotnie większym ryzykiem względnym rozpoznania zaburzeń psychicznych w obecnym momencie i w ciągu całego życia. Osoby z wysokim nasileniem objawów CASu różnią się także istotnie w zakresie połączeń funkcjonalnych w mózgu w kilku istotnych sieciach neuronalnych – sieci spoczynkowej, sieci wykonawczej i sieci istotności.

Uzyskane wyniki mogą wskazywać na istotną rolę wysokiego nasilenia objawów CASu w etiopatogenezie różnego rodzaju zaburzeń psychicznych, co potwierdza jedno z głównych założeń metapoznawczej teorii zaburzeń psychicznych i rozszerza je o dodatkową perspektywę różnic w funkcjonowaniu mózgu u osób z różnym nasileniem objawów CASu.

Słowa kluczowe: terapia metapoznawcza, przekonania metapoznawcze, depresja, lęk, PTSD, ruminacje, fMRI, resting state

Abstract

Cognitive-attentional syndrome is a key construct in the metacognitive approach to psychopathology and psychotherapy. It consists of maladaptive patterns of repetitive negative thinking and dysfunctional metacognitive beliefs. In this approach CAS is a transdiagnostic construct, involved in etiopathology of various psychological disorders.

Two scientific papers are presented in this dissertation. The main goal was to confirm the transdiagnostic status of cognitive-attentional syndrome. The first one concentrated on exploring the relationship between CAS and psychopathology symptoms and psychological disorders. The other one was concerned with the differences in neural functioning between people with high and low levels of CAS symptoms. This was done by means of rumination induction procedure and a resting state fMRI session.

CAS symptoms are related to higher levels of various psychopathology symptoms and several times higher relative risk of diagnosing both current and lifetime psychological disorders. People reporting high levels of CAS also differ significantly in the brain functional connectivity in some prominent brain neural networks – default mode, central executive and salience networks.

Results of this study indicate a prominent role that high levels of CAS symptoms may have in etiopathogenesis of various psychological disorders. This confirms one of the main assumptions of metacognitive theory of psychopathology. Plus to that, it provides an additional perspective of the differences in brain functioning between people reporting high and low levels of CAS symptoms.

Keywords: metacognitive therapy, metacognitive beliefs, depression, anxiety, PTSD, rumination, fMRI, resting state

Wprowadzenie

Niniejsza praca dotyczy syndromu-poznawczo uwagowego (*cognitive-attentional syndrome*, CAS), jego neuronalnych korelatów oraz związków z objawami psychopatologicznymi. Składają się na nią dwa artykuły opublikowane w anglojęzycznych recenzowanych czasopismach naukowych (pierwszy w *Comprehensive Psychiatry,* a drugi we *Frontiers in Psychology*, w numerze specjalnym poświęconym terapii w nurcie metapoznawczym – *Metacognitive Therapy: Science and Practice of a Paradigm*). Pierwsza praca obejmuje dwa badania korelacyjne na dużych próbach (n=1225 i 602) i badanie z udziałem n=98 osób z zastosowaniem strukturyzowanego wywiadu klinicznego. Druga praca to badanie z zastosowaniem funkcjonalnego rezonansu magnetycznego (fMRI), w kórym zastosowano dwie procedury badawcze – indukcję myślenia ruminacyjnego i pomiar aktywności spoczynkowej mózgu (rsfMRI), z udziałem n=55 osób. Ze względu na obszerność prezentowanego materiału zdecydowano się przedstawić te dwie prace jako cykl.

Podstawowym konstruktem teoretycznym, do którego odwołują się obie prace, jest syndrom poznawczo-uwagowy. Według metapoznawczego podejścia do zaburzeń psychicznych, opracowanego przez Adriana Wellsa (2009) i modelu samoregulującej funkcji wykonawczej autorstwa Wellsa i Matthewsa (1994, 1996), CAS jest zbiorem stylów czy strategii myślenia i zachowania, które wynikają z nieadaptacyjnych przekonań metapoznawczych. Te style myślenia obejmują wzorzec powtarzających się negatywnych myśli, dotyczących przeszłości i przyszłości – ruminacji i zamartwiania się – oraz koncentracji uwagi na zagrażających bodźcach – myślach, doznaniach cielesnych, sygnałach ze środowiska. Strategie behawioralne obejmują takie niekorzystne zachowania jak tłumienie myśli i emocji, próby kontrolowania myśli i doznań cielesnych, unikanie sytuacji, spożywanie alkoholu i sięganie po substancje psychoaktywne, proszenie innych o zapewnienia. Nieadaptacyjne przekonania metapoznawcze dzielą się na dwie kategorie: pozytywne i negatywne Przekonania pozytywne dotyczą oczekiwanych korzyści i zysków ze

strategii związanych z objawami CASu, np. "Dzięki ruminowaniu zrozumiem dlaczego taki jestem", "Zamartwianie się pozwala mi być przygotowanym na najgorsze", "Jeśli będę kontrolował swoje myśli o tym jak mi źle, to poczuję się lepiej". Tymczasem, przekonania negatywne dotyczą przede wszystkim braku kontroli nad myślami i spodziewanych w związku z tym zagrożeń, np. „Nie jestem w stanie pracować, kiedy cały czas się zamartwiam", „Jeśli nie mam kontroli nad myślami, to znaczy, że jestem nieprzewidywalny", „Rozchoruję się jeśli będę cały czas myślał w ten sposób".

Tematyka syndromu-poznawczo uwagowego została podjęta z kilku powodów. Pierwszym jest rosnąca popularność podejść do psychopatologii i psychoterapii w nurcie metapoznawczym (Moritz i Lysaker, 2018, Moritz, Lysaker, Hofmann i Hautzinger, 2018), a szczególnie obiecujące wydają się być wyniki badań dotyczące skuteczności terapii metapoznawczej stworzonej przez Adriana Wellsa (Normann i Morina, 2018). Niezwykle ważnymi elementami rozwoju podejścia do terapii jest weryfikacja założeń teoretycznych danego modelu oraz jakości i użyteczności narzędzi pomiarowych używanych w badaniach nad tym podejściem. Prezentowane tutaj artykuły dotyczą tej problematyki. Taką kwestią może być namysł nad stosowanymi dotąd sposobami pomiaru nasilenia objawów CASu i trafność różnego rodzaju pomiarów. Kluczowym zaś aspektem eksplorowanym i dyskutowanym w przedstawionych tu pracach jest transdiagnostyczny status CASu, który wedle teorii Wellsa (2009) leży u podłoża zaburzeń, przede wszystkim emocjonalnych: depresyjnych i lękowych oraz zaburzenia po stresie traumatycznym (*post-traumatic stress disorder*, PTSD), ale także na przykład zaburzeń obsesyjno-kompulsyjnych. Prezentowane w tej pracy badania dotykają tej problematyki poprzez eksplorację związków nasilenia CASu z objawami psychopatologicznymi i ustalenie diagnoz klinicznych u osób z wysokim i niskim nasileniem objawów CASu oraz badanie neuronalnych korelatów tego syndromu. Określenie charakterystyki syndromu przez badanie jego mózgowego podłoża zazębia się z nowoczesnymi, wielowymiarowymi podejściami do psychopatologii, w których poza

obrazem klinicznym analizuje się również dane biologiczne czy neurofizjologiczne, łącząc je we wspólną konceptualizację. Przykładem takiego podejścia może być zapowiedziany i realizowany przez National Insitute of Mental Health z USA projekt *Research Domain Criteria* (RDoC) (Cuthbert, 2014), w którym deficyty i zaburzenia w kluczowych obszarach funkcjonowania (np. procesy poznawcze, jak uwaga, czy systemy społeczne jak formowanie więzi i przywiązania) mają być konceptualizowane na różnych poziomach, od korelatów genetycznych, poprzez komórki, sieci neuronowe, reakcje fizjologiczne i zachowanie aż po obserwacje pochodzące z samoopisu.

Pierwsza prezentowana tutaj praca, obejmująca łącznie aż trzy badania, miała na celu ukazać właściwości psychometryczne kwestionariusza CAS-1, służącego do pomiaru nasilenia objawów CASu, jego struktury czynnikowej oraz, przede wszystkim, związków z objawami psychopatologicznymi. Miała również odpowiedzieć na pytanie dotyczące sposobów pomiaru CASu, jako że w literaturze obecne są dwa sposoby – łączenie miar ruminacji/zamartwiania się i przekonań metapoznawczych lub stosowanie samodzielnie kwestionariusza CAS-1. Właściwości narzędzia okazały się ogólnie zadowalające. Wykazano, że łączenie różnych narzędzi do pomiaru CASu pozwala na lepszą predykcję nasilenia objawów psychopatologicznych niż sam kwestionariusz CAS-1. W celu eksploracji związków z zaburzeniami psychicznymi przeprowadzono badanie korelacyjne na dużej próbie (N=602), gdzie wykorzystano kwestionariusze objawów psychopatologicznych i jakości życia, oraz badanie na próbie niemal 100 osób z zastosowaniem wywiadu standaryzowanego SCID-I. Badanie korelacyjne wykazało umiarkowanie silne pozytywne związki między nasileniem objawów CASu i wszystkimi rodzajami mierzonych objawów psychopatologicznych. Wyniki te są zgodne z wcześniejszymi pracami, głównie dotyczącymi objawów i zaburzeń depresyjnych i lękowych (np. Fergus i wsp. 2012, 2013) oraz zaburzeń snu (Fergus i Scullin, 2017) oraz wskazały na związki między nasileniem objawów CASu i innymi rodzajami objawów psychopatologicznych, np. objawami wytwórczymi, uzależnień,

manii, zaburzeń jedzenia, funkcji poznawczych czy seksualnych. Doprowadziły też autorów do dyskutowanych w tej pracy hipotez, których mogą dotyczyć przyszłe badania, np. CASu jako moderatora między czynnikami ryzyka albo mechanizmami psychopatologii a wystąpieniem lub nasileniem objawów. Przeprowadzone badania potwierdzają zdecydowane związki CASu z niemal każdym mierzonym nasileniem objawów w populacji ogólnej. Może to wskazywać na rolę CASu w formowaniu zaburzeń, gdzie interakcja czynników ryzyka i poziomu CASu jest w zależności moderacji – im wyższy poziom CASu, tym silniejsza zależność między wystąpieniem czynnikiem ryzyka psychopatologii a diagnozą zaburzenia. W innej pracy, nie ujętej w tym cyklu, analizowane są związki między poziomem CASu, obecnością diagnozy klinicznej i historią traumatycznych doświadczeń w dzieciństwie (Dragan i Kowalski, w recenzji). Wyniki tego badania zdają się potwierdzać tę relację – wysoki poziom CASu i obecność traum w wieku dziecięcym są silnie związane z obecnością diagnozy zaburzeń emocjonalnych (87% badanych z tej kategorii), zaś osoby z niskim poziomem CASu i doświadczeniem traum były nawet rzadziej diagnozowane niż osoby bez takiego doświadczenia i wysokim poziomem CASu (19% versus 31%), co może wskazywać na istotną rolę CASu w rozwoju zaburzeń albo obecność innych, niebadanych czynników ryzyka.

Ostatnie badanie z pierwszego prezentowanego w tej pracy artykułu - badanie z zastosowaniem wywiadu klinicznego, polegające na określeniu diagnoz psychiatrycznych w grupie osób z niskim i wysokim nasileniem objawów CASu, wykazało, że w tej drugiej grupie od kilku do kilkunastu razy częściej mogą być diagnozowane zaburzenia psychiczne. Ryzyko względne wyniosło RR=6.34 (CI 95%=2.91–13.80) dla diagnozy w ciągu życia i RR= 7.36 (CI 95%= 2.32–23.39) dla obecnej diagnozy. Rozpoznawane były przede wszystkim zaburzenia depresyjne i lękowe oraz zaburzenie po stresie traumatycznym, ale również zaburzenia związane z nadużywaniem substancji i zaburzenia odżywiania.

Jak wykazano w części przeglądowej w drugiej z prac składających się na

przedstawiony cykl publikacji, zaburzenia emocjonalne, tj. depresyjne i lękowe, oraz PTSD wiążą się ze zmienionymi wzorcami funkcjonowania mózgu w obszarach związanych z emocjami (*emotion processing*), myśleniem na własny temat (*self-referential processing*) i celowym funkcjonowaniem poznawczym (*task-oriented processing*) (meta-analizy: Hamilton i wsp., 2012; Palmer, Crewther, Carey i wsp., 2015; Ipser, Singh i Stein, 2013; Simmons & Matthews, 2012). W związku z tym, że - jak wykazano we wcześniejszej pracy - wysokie nasilenie objawów CASu powiązane jest z kilku- do kilkunastokrotnie zwiększonym ryzykiem względnym rozpoznania zaburzeń psychicznych, postanowiono eksplorować neuronalne korelaty tego syndromu w obszarach mózgu szczególnie związanych z ruminacyjnym stylem myślenia, istotnym elementem CASu, oraz wskazanych w wymienionych wcześniej meta-analizach jako obszary zmienionego funkcjonowania mózgu u osób z zaburzeniami psychicznymi. Przeprowadzono badanie osób wybranych z dużej próby (N=1225) ze względu na niski (n=33) bądź wysoki (n=25) i stały w czasie poziom nasilenia objawów CASu. Zastosowano dwie metody badania fMRI – zadanie z indukcją myślenia ruminacyjnego (zmodyfikowana procedura badania z udziałem osób z depresją – Cooney i wsp., 2010) oraz pomiar aktywności spoczynkowej mózgu (*resting state*). Procedura indukcji ruminacji obejmowała jako warunek kontrolny również zadanie z myśleniem abstrakcyjnym, w którego przetwarzaniu mózgowym również odkryto różnice między grupami, co stanowi znaczące rozszerzenie danych dotyczących wykorzystanej procedury, w którym różnice w zakresie myślenia abstrakcyjnego u osób z depresją nie były w ogóle analizowane i raportowane (Cooney i wsp., 2010). Wyniki analizy połączeń funkcjonalnych (*functional connectivity*) w tych dwóch procedurach badawczych wykazały zmienione wzorce połączeń funkcjonalnych w obszarach związanych z przetwarzaniem emocji, myśleniem i przetwarzaniem informacji na własny temat oraz przetwarzaniem związanym z zadaniami. Obszary te przynależą do głównych sieci funkcjonalnych identyfikowanych w ludzkim mózgu – sieci spoczynkowej (*default mode network*),

centralnej sieci wykonawczej (*central executive network*) i sieci istotności (*salience network*).

Podsumowując, pierwszy artykuł obejmuje trzy badania, dwa korelacyjne na dużych próbach i jedno porównawcze z przeprowadzeniem diagnozy klinicznej, drugi zaś obejmuje badanie fMRI z zastosowaniem dwóch procedur – indukcji ruminacji i myślenia abstrakcyjnego i pomiaru aktywności spoczynkowej mózgu. Pierwszy artykuł wskazuje na szerokie i stosunkowo silne związki nasilenia objawów CASu z różnego rodzaju objawami psychopatologicznymi, jak również wielokrotnie zwiększone ryzyko względne rozpoznania zaburzeń psychicznych u osób z wysokim poziomem objawów CASu w porównaniu do osób z ich niskim poziomem. Z kolei badanie z zastosowaniem fMRI wskazuje na różnice w funkcjonowaniu mózgu między osobami z wysokim i niskim nasileniem objawów CASu – zarówno w zakresie podstawowych sieci neuronalnych i przetwarzania emocji czy informacji o sobie, jak również przetwarzania związanego z zadaniami. Wyniki przedstawionych w tych pracach badań stanowią argument za metapoznawczym modelem zaburzeń psychicznych, w których wysoki poziom objawów CASu jest czynnikiem leżącym u podłoża różnego rodzaju zaburzeń emocjonalnych.

Zaprezentowane w tej pracy badania mają swoje ograniczenia. Są to badania korelacyjne i głównie porównawcze, które nie pozwalają na wyciąganie wniosków o charakterze przyczynowo-skutkowym, jeśli chodzi o rolę CASu w etiopatogenezie zaburzeń psychicznych. Jednocześnie stanowią uzupełnienie luk w istniejącej literaturze przedmiotu dotyczącej metapoznawczego podejścia do psychopatologii. Według wiedzy autora zaprezentowano tutaj pierwsze badanie, w którym formalnie diagnozowano osoby z różnym nasileniem objawów CASu oraz pierwsze badanie mózgowych korelatów CASu. Stanowią one znaczący wkład w potwierdzenie transdiagnostycznego statusu CASu – powtarzającego się negatywnego myślenia i nieadaptacyjnych przekonań metapoznawczych – jako czynnika ryzyka rozwoju zaburzeń psychicznych różnego rodzaju, szczególnie zaburzeń depresyjnych

i lękowych. Wykrycie różnic w mózgowej aktywności u osób z wysokim i niskim nasileniem CASu, które obejmują różnego rodzaju sieci funkcjonalne, jest zgodne z założeniami metapoznawczego modelu psychopatologii i stanowi jego rozwinięcie.

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Cognitive-attentional syndrome – The psychometric properties of the CAS-1 and multi-measure CAS-based clinical diagnosis

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ABSTRACT

The Cognitive-attentional Syndrome Questionnaire (CAS-1) is a short self-descriptive measure developed to provide information regarding the severity of cognitive-attentional syndrome, a key construct in metacognitive therapy. The three presented studies explore the psychometric properties of the CAS-1. Study 1 was based on a community sample ($N = 1225$) and explored the factor structure of the CAS-1, its relations with measures of rumination and metacognitive beliefs, and its demographic structure. Study 2, performed on an internet-based sample ($N = 602$), explored relations of the CAS-1 with measures of rumination, psychopathology, and quality of life. This study also dealt with the validity of the CAS-1. Study 3 was conducted on participants selected from study 1 ($n = 98$), based on the results of the CAS-1 and other measures. It explored the predictive validity of the questionnaire's diagnosis through ascertaining clinical diagnoses. All three studies confirm the reliability of the CAS-1. Its validity was confirmed by significant associations with measures of rumination, metacognitive beliefs, psychopathology, and quality of life. Two-factor and four-factor structures of the CAS-1 were confirmed, with the two-factor model better fitting the data. The results obtained show that the CAS-1 has good psychometric properties; its current form is deemed most acceptable for clinical use and we advise use of combined measures of CAS or development of a more expanded measure of CAS for research purposes.

1. Introduction

Cognitive-attentional syndrome (CAS) is a core aspect of Wells' metacognitive approach to psychopathology and the metacognitive therapy (MCT) of emotional disorders [1–3]. It consists of three aspects: 1) repetitive negative thinking, i.e. rumination and worry; 2) focusing attention on threats (external – e.g. a person with social anxiety disorder paying attention to any display of vexation amongst peers, or internal – e.g. a person with panic disorder scanning their bodily functions in search of threatening signals like elevated heart rate); and 3) maladaptive, paradoxically inefficient behaviors and strategies used to cope with the first two aspects (e.g. thought suppression, thought and situation avoidance, or substance/alcohol use). These thinking and behavior patterns have been observed and interpreted as the cause of psychological problems in a plethora of clinical and population-based studies [e.g. 3–8]. CAS results from maladaptive positive ('worrying helps me cope') and negative ('worrying will ruin my health') metacognitive beliefs and corresponding schemas and meta-strategies, which are reversibly solidified by elevated levels of CAS [2,9–14]. Thus metacognitive beliefs are also central to CAS. This syndrome has a central role in the self-regulatory executive function model (S-REF) developed by Wells & Matthews [1,4]. According to this model, self-regulatory executive function becomes activated when there is a discrepancy between self-relevant goals (outer circumstances and mental states) and perceived goals. In most people, periods of CAS activation – and therefore negative emotions, self-appraisal, and sense of threat – will be brief or non-existent. However, some will experience prolonged CAS activation, which is understood in the S-REF model as the cause of emotional and other psychiatric disorders or their core, common component. Therefore, CAS is seen as a basic and transdiagnostic factor of psychological disturbances, especially emotional disorders (e.g. mood and anxiety disorders), but it is also possible that other types of psychiatric symptoms are intensified by elevated levels of CAS. Prolonged CAS activation may result from its vicious-circle characteristic: for example, a person with income- and poverty-related anxiety after losing their job engages in negative repetitive thoughts on the causes (rumination) and consequences (worry) of the event, resulting from positive metacognitive beliefs (e.g. 'this thinking will help me understand and prepare'). Consequently, this person may experience loss of performance due to their attention resources being engaged by CAS or simply find that they are devoting excessive

Abbreviations: CAS, cognitive-attentional syndrome; CAS-1, Cognitive-Attentional Syndrome questionnaire; MCT, metacognitive therapy; MCQ-30, Metacognitions Questionnaire 30; RRS, Ruminative Response Scale.

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amounts of time to worry and rumination. This observation may trigger worrying about worrying [cf. 3] due to negative metacognitive beliefs (e.g. 'I won't be able to work if I constantly worry'). Strategies like attempting to suppress thoughts about having lost a job or avoiding job-related topics will probably lead to greater preoccupation with these thoughts, meaning that CAS is likely to continue to occur.

The Cognitive-attentional Syndrome Questionnaire (CAS-1) was developed to measure aspects of CAS, with its primary goal being use in clinical practice [2] (note: cognitive-attentional syndrome – the theoretical construct – is abbreviated as CAS and the questionnaire which measures it was named the CAS-1 by Wells [2]; these abbreviations are used in this paper). It was devised as a short tool for assessing general levels of CAS without disorder-specific symptomatology. To date, there have been three studies which have used the CAS-1 [15–17]. The first study [15] was conducted on a student sample and revealed relationships between CAS and anxiety, depression, and stress as well as the moderating role of beliefs about attentional control in these relationships – beliefs about low attention control produced stronger relationships between elevated CAS and psychopathology symptoms. The second study [16] was conducted on a sample of patients with emotional disorders (primarily mood or anxiety disorders). It revealed relationships between CAS and depressive and anxiety symptoms as well as the incremental validity of the CAS-1 when controlling for psychological inflexibility. The third study [17] established a relationship between CAS, especially maladaptive strategies and negative metacognitive beliefs, and sleep disturbances.

It seems important for the diagnostic use of the CAS-1 to detail its psychometric properties in a large community sample and to analyze gender and age differences. It is hypothesized that female participants will have higher levels of CAS as they are more often afflicted with depressive [18] and anxiety [19] disorders. Emotional disorders are a primary interest in metacognitive models, however the psychological mechanisms they describe might not be universal across other disorders. For example, men are more often affected by substance/alcohol-abuse disorders [20]. It is assumed that such disorders might be related to a slightly different set of metacognitive beliefs [21,22], mostly concerning the role of alcohol/substances in emotional regulation. A large epidemiological study in a Polish sample [23] revealed similar gender differences in emotional disorders and substance/alcohol-related disturbances. In light of mixed results concerning the differing prevalence of disorders in different age groups in the Polish population [23], it is hypothesized that the null-hypothesis of no differences in CAS levels between age groups will hold. The predictive value of the CAS-1 is also important for validating the transdiagnostic status of CAS [cf. 16]. The theoretical model proposed by Wells and Matthews [2,24] implies that people with high and/or frequent CAS activation are prone to developing emotional disorders. We aim to test this implication of S-REF theory. The aforementioned studies, and others [10–12], work backwards because they explore CAS (mostly as a combination of metacognitive beliefs, rumination tendencies, or worrying) in patients with established diagnoses, especially depression and generalized anxiety disorder (GAD). A second group of studies explore levels of symptoms, but without full clinical examination [9,12,13]. To date, there have been no studies exploring various psychiatric disorders in people with high CAS levels. As mentioned above, most studies validating metacognitive models of disorders did not use the CAS-1, instead they mostly used a combination of the metacognitions questionnaire (MCQ-30) [25] and rumination or worry questionnaires for depression and anxiety models, respectively. Thus, it is of interest to measure the validity of the CAS-1 in predicting the symptoms of various psychological disorders when controlling for the results of metacognition, rumination, or worrying questionnaires [26]. The hypothesis here is that the CAS-1 could serve as a stand-alone measure of all elements of CAS, predicting a high percentage of the variance of general psychopathology and emotional disorder symptoms. Because different methods of assessing CAS were used in previous studies [9–13,15–17], testing this hypothesis will allow the issue of various measures of CAS being used in research to be addressed. Examining the factorial structure of the CAS-1 is also of interest [16]. The CAS-1, as a comprehensible measure of CAS, should consist of four factors (worry/rumination, attention to threat, CAS-related behaviors, and metacognitive beliefs) which will load one main factor – CAS, according to Wells's metacognitive theory [2]. Repetitive negative thinking (i.e. worry/rumination) and attention to threat may be viewed as functioning strategies [24], as may the strategies and behaviors listed separately in the CAS-1, thus it is important to test a model in which these items are grouped together in such a fashion. Also, metacognitive beliefs are conceptually divided into positive and negative beliefs, which should also be reflected in factor analyses. Thus, in the present paper we examine 2-, 3-, 4-, and 5- factor models of the CAS-1 and compare them against each other.

Three studies are presented in this paper. The first study deals with the convergent validity of the CAS-1 and age and sex differences in cognitive-attentional syndrome levels in a large sample mirroring the population of a large city. The factorial structure of the CAS-1 is also explored in this study. The second study concerns the convergent validity of the CAS-1, its relationships with different types of psychopathology symptoms and quality of life, as well as the validity of this questionnaire in predicting levels of psychopathology symptoms, taking into account the rumination and metacognitive beliefs questionnaires. The third study, conducted on a pre-selected sample of people with high and low CAS scores, concerns the predictive validity of CAS as a theoretical construct through ascertaining clinical diagnoses in both groups.

2. Study 1

2.1. Procedure and sample characteristics

The study was conducted through an internet survey panel. The panel participants are offered financial and/or material rewards for participation in different survey studies. In this study, the participants were additionally motivated by the possibility of a large financial reward (about 50 EUR) for participation in the second stage of the study.

The sample was gathered for the purpose of a further fMRI study, so there were strict exclusion criteria: a history of head trauma and psychiatric and neurological disorders, substance dependence, metal objects within the body, being pregnant, having irremovable piercings, tattoos on the head area, left-handedness, claustrophobia, serious medical procedures in the past two years, and sundry medical equipment such as artificial pacemakers, bypasses, stents, etc. Participants were also required to live in Warsaw and the surrounding area to ensure their ability to participate in further stages of the study. Fig. 1 shows a consort flowchart of the recruitment of participants.

A total of 1225 participants were eligible and completed the study. The dropout rate was 36%. Participants were selected based on quotas mirroring the population of Warsaw [27,28] in terms of sex, age, and education. However, the final demographic structure of the obtained sample was slightly different to Warsaw's population: 52% females in the population vs 61% in the study sample; 27% people aged 18–29, 42% aged 30–39, and 31% aged 40–50 in the population vs 38%, 39%, and 23% respectively in the study sample; the demographic was also shifted in favor of higher education, with 53% of the population having higher education vs 64% in the study sample. The characteristics of the final sample are presented in the results section.

2.2. Method and measures

2.2.1. The Cognitive-Attentional Syndrome Questionnaire (CAS-1)

The CAS-1 [2] questionnaire consists of 16 items. The first two, assessed on a scale from 0 to 8, are questions concerning the frequency of rumination and worry as well as concentration on threats. A further six items, assessed on a scale from 0 to 8, concern maladaptive behaviors used to cope with negative emotions and/or thoughts, e.g. thought

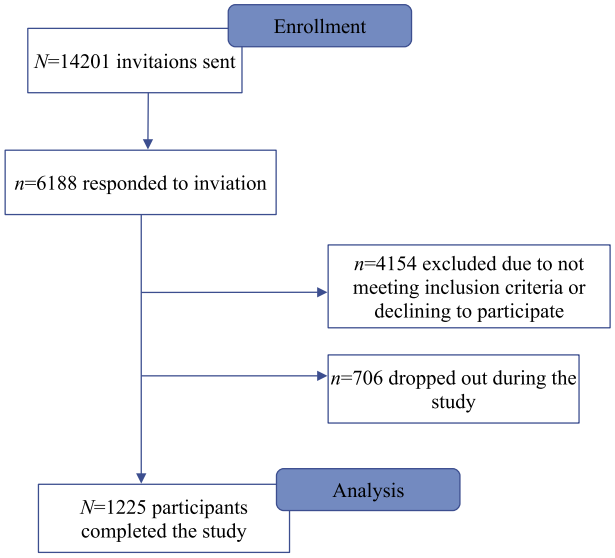

Fig. 1. Consort flow chart for recruitment for the first study.

and situation avoidance, drinking or substance abuse, and attempts to control thoughts or emotions. The last eight items, assessed on a scale from 0 to 100, concern positive and negative metacognitive beliefs core to cognitive-attentional syndrome: e.g. "worrying too much could harm me" or "worrying helps me cope". The results of the questionnaire were calculated as in the paper by Fergus et al. [15] – the last eight items were recalculated to range between 0 and 8 before being summed up. The total results can range from 0 to 128, where a higher result indicates a greater level of cognitive-attentional syndrome. The Polish version was prepared in cooperation with the author of the original scale and translated into Polish with the use of the back-translation procedure.

2.2.2. Ruminative Response Scale (RRS)

The 22-item Ruminative Response Scale was originally extracted from the 71-item Response Styles Questionnaire [29]. It focuses on one's responses to depressive mood: concentration on the self, symptoms, and the causes and consequences of depressive mood. A newer approach excludes from the scale items which are too highly correlated with depression measures and distinguishes two subscales: a "Reflection" subscale, which captures the contemplative and problem-solving nature of self-focused thinking, and a "Brooding" subscale, which is defined as moody and gloomy pondering [30]. The "Brooding" and "Reflection" subscales both consist of 5 items, with results ranging from 4 to 20, where a higher result indicates higher levels of a particular response to depressed mood. The Polish version of the RRS (revised) has generally good psychometric qualities [31]. In the current study, the RRS had excellent internal consistency of $\alpha = 0.94$ and the subscales had acceptable internal consistency: Brooding $\alpha = 0.83$ and Reflection $\alpha = 0.76$.

2.2.3. Metacognitions Questionnaire 30 (MCQ-30)

The short version of the Metacognitions Questionnaire, developed by Wells and Cartwright-Hatton [25], consists of five subscales and 30 items. It concerns metacognitive beliefs: monitoring techniques, judgments, and beliefs about one's thoughts and cognitive abilities essential in the metacognitive model of psychopathology. The "Cognitive Confidence" subscale concerns one's beliefs about insufficient cognitive abilities, e.g. "I have a poor memory". The "Positive Beliefs" subscale consists of items about the advantageous qualities of worry, e.g. "Worrying helps me cope". The "Cognitive Self-consciousness" subscale concerns one's tendency to monitor cognition, e.g. "I constantly examine my thoughts". The fourth subscale, "Uncontrollability and Danger", explores the negative aspects of worry, e.g. "I could make myself sick with worrying". The final subscale is about the "Need to Control Thoughts", e.g. "I should be in control of my thoughts all the time". The Polish version of this questionnaire exhibits good psychometric qualities and is considered equivalent to the English version [32]. In this study, the MCQ-30 had an excellent internal consistency of $\alpha = 0.91$ and its subscales had acceptable internal consistency, with α values ranging from 0.76 to 0.88.

2.2.4. Method

This study was designed as a correlative study and was based on a large sample mirroring the population of a big city. The validity of the CAS-1 was tested with a linear regression model with demographic variables as well as RRS and MCQ-30 scores as predictors. A univariate ANOVA with two-way interaction was performed to examine age and gender differences in CAS-1 scores. These statistics were calculated with SPSS 24 software. Effect sizes were calculated with an online calculator (https://www.psychometrica.de/effect_size.html), accounting for group size differences. The factor structure of the CAS-1 was analysed with confirmatory factor analysis in AMOS 24 software with comparative fit index (CFI) and root mean square error of approximation (RMSEA) used as fit indices. The Bayesian Information Criterion (BIC) [33] was used to compare structural models against each other.

2.3. Results of study 1

The CAS-1 had an internal consistency of Cronbach's $\alpha = 0.85$. Mean results and standard deviations of the questionnaires and their subscales were as follows: CAS-1: 55.69 (18.90), RRS: 19.48 (5.77), RRS-Brooding: 10.09 (3.34), RRS-Reflection: 9.38 (3.03), MCQ-30: 58.78 (14.39), Cognitive Confidence: 11.73 (4.46), Positive Beliefs: 9.18 (3.64), Cognitive Self-consciousness: 13.15 (3.78), Uncontrollability and Danger: 13.00 (4.20), and Need to Control Thoughts: 11.74 (3.81). A univariate ANOVA revealed a significant difference in CAS-1 levels between males and females: $F(1, 1219) = 13.18$, $p > 0.001$ with a small effect size $d = 0.2$ (CI 95% = 0.09–0.32). There was no simple main effect of age with CAS-1 levels: $F(2, 1219) = 2.05$, $p = 0.13$. There were no significant results for interaction of gender and age with CAS-1 levels $F(2, 1219) = 1.57$, $p = 0.21$. A linear regression model with CAS-1 scores as response and with demographic variables and RRS and MCQ-30 subscales as predictors was created to verify the validity of the CAS-1: $F(9, 1215) = 124.24$, $p < 0.001$, $R^2 = 0.48$. Details of the model are shown in Table 1.

The confirmatory factor analyses were performed with AMOS for SPSS (version 24). We created 2-, 3-, 4-, and 5-factor models; their details (fit indices and factor loadings) are presented in Table 2. In each model, Modification Indices of M.I. ≥ 40 were deemed suitable for introducing intercorrelation between item errors to maximize the fit of the models to the data while simultaneously avoiding overfitting and ensuring that conditions for all tested models were similar. Analysis of BIC indices for different models revealed that the 2-factor and 4-factor models are characterized by the lowest values of this measure (i.e. the

Table 1
Details of linear regression analysis with CAS-1 as response variable and with demographic and questionnaire measures as predictors.

Response variable: CAS-1		β	t	p
Age		0.05	2.22	0.027
Gender		−0.04	−1.94	0.053
RRS subscales	Brooding	0.22	7.53	<0.001
	Reflection	0.17	5.39	<0.001
MCQ-30 subscales	Cognitive Confidence	−0.04	−1.47	0.14
	Positive Beliefs	0.16	6.41	<0.001
	Cognitive Self-consciousness	0.02	0.63	0.53
	Uncontrollability and Danger	0.23	7.78	<0.001
	Need to Control Thoughts	0.13	4.30	<0.001

best fit for the obtained data). Of these two models, the 2-factor model appears to be the better fit, $\Delta BIC = 8.35$.

2.4. Conclusions

These results indicate the satisfactory validity and reliability of CAS-1 measures. They also shed light on gender differences in CAS levels, with women obtaining higher scores. The analyses performed also indicate that the theory driven [2] 2-factor and 4-factor structures of the CAS-1 are acceptable and are of good fit to the obtained data, in contrast to the 3- and 5-factor models, which are also based on theory.

3. Study 2

3.1. Procedure and sample characteristics

The study was conducted via an internet tool for online surveying – LimeSurvey. Links to the study were shared across social media – especially clinical psychology and neuropsychology fan-pages and students' groups on Facebook. Invitations to the study were supplemented with requests to distribute the study to one's social contacts. Therefore the sampling technique can be characterized as a mix of convenience and snowball sampling. A total of 1080 people took part in the study, and 602 people completed all measures. The dropout rate was 44%, which was not unexpected due to the length of the study. Only completed surveys were included in the analyses.

The sample had a mean age of 31.92 ($SD = 10.18$) with a range from 18 to 75 years. Approximately 77% of the participants were female; 1.5% of participants did not report their gender identification. Approximately 71% of the participants reported having higher education, 25% had secondary education, and the rest reported basic or vocational education. 18.3% of participants declared living in a small town with a population of up to 20 thousand, 18.4% participants declared living in a medium-sized town with between 20 and 100 thousand inhabitants, and 63.3% of participants lived in a large city with a population above 100 thousand. The use of the services of a psychiatrist, psychologist, or psychotherapist at the time of the study was reported by 18.8% of participants. This is in-line with data from research on the prevalence

Table 2
Results of factor analyses of CAS-1.

Models and their fit indices					
		2 factors	3 factors	4 factors	5 factors
CFI		0.92	0.91	0.92	0.91
RMSEA		0.068	0.071	0.068	0.72
χ^2		617.94	683.52	626.29	694.76
BIC		923.70	975.06	932.05	986.30
Items and their factor loadings					
1. How much time in the last week have you found yourself dwelling on or worrying about your problems?		0.64	0.62	0.79	0.78
2. How much time in the last week have you been focusing attention on the things you find threatening (e.g., symptoms, thoughts, danger)?		0.68	0.65	0.84	0.83
How often in the last week have you done the following in order to cope with your negative feelings or thoughts?	3. Avoided situations	0.71	0.70	0.72	0.72
	4. Tried not to think about things	0.67	0.66	0.68	0.68
	5. Used alcohol/drugs	0.38	0.36	0.40	0.37
	6. Asked for reassurance	0.67	0.66	0.67	0.67
	7. Tried to control my emotions	0.53	0.53	0.53	0.53
	8. Tried to control my symptoms	0.63	0.63	0.63	0.64

Table 2 (*continued*)

Below are a number of beliefs people have. Indicate how much you believe each one by placing a number from the scale below next to each item.	9. Worrying too much could harm me	0.35	0.37	0.34	0.36
	10. Strong emotions are dangerous	0.43	0.43	0.42	0.42
	11. I cannot control my thoughts	0.71	0.73	0.72	0.75
	12. Some thoughts could make me lose my mind	0.70	0.71	0.70	0.70
	13. Worrying helps me cope	0.43	0.59	0.43	0.59
	14. Focusing on possible threats can keep me safe	0.34	0.76	0.34	0.76
	15. It is important to control my thoughts	0.35	0.46	0.33	0.45
	16. Analyzing my problems will help me find answers	0.14	0.40	0.14	0.40

CAS-1 – Cognitive-attention Syndrome Questionnaire, CFI – Comparative Fit Index; RMSEA – Root Mean Square Error of Approximation. Cell colors indicate belonging to certain factors.

of mental health problems in the Polish population [23] and allows the sample to be considered a community based one.

3.2. Method and measures

The study employed the assessment tools used in the previous study: the CAS-1, the RRS (in this study, the "Brooding" and "Reflection" subscales had acceptable internal consistency, $\alpha = 0.77$ and 0.73 respectively), and the MCQ-30 (which had excellent internal consistency in this study, $\alpha = 0.90$; its subscales' consistencies were acceptable, with α's ranging from 0.77 to 0.89). It also employed other measures, described in detail below.

3.2.1. The General Functioning Questionnaire (GFQ-58)

The General Functioning Questionnaire [34] is a checklist-type questionnaire concerning general functioning and different types of psychopathology symptoms. It consists of 13 subscales with a total of 58 items. Three concern general functional aspects: poor functioning in the workplace and at home, lack of entertainment, and poor social relations. Ten subscales concern various types of symptoms: cognitive impairments, addictions, positive psychotic symptoms (delusions and hallucinations), depressive symptoms, manic symptoms, anxiety symptoms, eating disorder symptoms, sleep problems, sexual disorders, and somatic symptoms. The number of items for subscales varies and can range from 2 (sexual disorders) to 8 (anxiety disorders), with most scales having 4 or 6 items. The total result can vary from 58 to 290 points, where higher results indicate greater levels of psychopathology symptoms. In the present study, the questionnaire had good internal consistency ($\alpha = 0.89$), the internal consistencies of separate subscales are presented elsewhere [34]. Only results concerning symptom subscales (without functioning subscales) are presented in this study.

3.2.2. The WHO Quality of Life Questionnaire - short version (WHOQOL-BREF)

WHOQOL-BREF is a 26-item questionnaire developed for measuring quality of life in four domains: physical health, social relationships, and psychological and environmental dimensions [35]. The total score on this questionnaire ranges from 26 to 130, where higher scores indicate greater quality of life. The Polish version of this questionnaire has acceptable psychometric properties [36]. In the present study, this questionnaire had good internal consistency ($\alpha = 0.89$). The psychological domain, the only subscale presented here, also had good internal consistency: $\alpha = 0.87$.

3.2.3. Method

This study was designed as a correlative study. The convergent validity of the CAS-1 was tested with a linear regression model with demographic variables, and CAS-1, RRS, and MCQ-30 scores as predictors of various psychopathology symptoms and quality of life. These statistics were calculated with SPSS 24 software.

3.3. Results of study 2

The mean values of the measures used were as follows: RRS = 45.45 ($\pm$12.47), MCQ-30 = 59.43 ($\pm$14.38), GFQ-58 = 117.00 ($\pm$83.80), CAS-1 = 55.17 ($\pm$19.70), WHOQOL-BREF = 83.80 ($\pm$15.85). In this study, the CAS-1 had internal consistency of $\alpha = 0.83$. The convergent validity of the CAS-1 was checked by creating regression models with demographic variables and CAS-1 scores as predictors of GFQ-58 symptoms subscales, the psychological domain, and total score of WHOQOL-BREF. These data are presented as Step 1 in Table 3. The second step in the regression analysis was to explore the predictive value of the CAS-1 for demographic variables and measures of rumination and

Table 3
Results of study 2; variance of different psychopathology symptoms and quality of life as explained by different CAS measures.

			Step 1			Step 2									
			sex	Age	CAS-1	Sex	Age	CAS-1	RRS-B	RRS-R	MCQ-1	MCQ-2	MCQ-3	MCQ-4	MCQ-5
WHOQOL-BREF	Total score	partial *r*	0.02	-0.22*	-0.57*	-0.04	-0.22*	-0.25*	-0.30*	-0.13°	-0.16*	-0.04	0.14*	-0.14*	-0.03
		R^2	0.33*			0.48*									
	Psychological domain	partial *r*	0.01	-0.06	-0.57*	-0.06	-0.06	-0.25*	-0.33*	-0.14*	-0.15*	-0.02	0.17*	-0.14*	-0.03
		R^2	0.32*			0.50*									
GFQ-58	Total score	partial *r*	-0.06	0.08	0.67*	0.00	0.07	0.33*	0.31*	0.16*	0.21*	0.01	-0.06	0.19*	0.07
		R^2	0.45*			0.61*									
	Somatic Symptoms	partial *r*	-0.14*	0.17*	0.45*	-0.10†	0.14*	0.20*	0.16*	0.03	0.17*	-0.03	0.04	0.11°	-0.08
		R^2	0.22*			0.29*									
	Sexual Disorders	partial *r*	-0.14*	0.21*	0.38*	-0.12°	0.20*	0.16*	0.09†	0.07	0.09†	0.03	-0.02	0.02	0.03
		R^2	0.17*			0.20*									
	Sleep Problems	partial *r*	-0.02	0.10†	0.42*	0.00	0.09†	0.16*	0.17*	0.04	0.08	-0.04	-0.01	0.06	0.06
		R^2	0.17*			0.22*									
	Eating Disorders Symptoms	partial *r*	-0.13*	-0.02	0.37*	-0.11°	-0.03	0.14*	0.15*	0.02	0.06	0.07	-0.05	0.06	0.01
		R^2	0.15*			0.19*									
	Anxiety Symptoms	partial *r*	-0.10†	0.06	0.63*	-0.04	0.04	0.28*	0.17*	0.09†	0.11°	0.05	0.01	0.28*	0.04
		R^2	0.40*			0.52*									
	Manic Disorders	partial *r*	0.00	-0.10†	0.47*	0.02	-0.10†	0.15*	0.14*	0.06	0.08	0.03	0.13°	0.07	0.09†
		R^2	0.23*			0.32*									
	Depressive Disorders	partial *r*	-0.06	0.07	0.62*	0.01	0.09†	0.30*	0.31*	0.17*	0.06	0.00	-0.08†	0.14*	0.02
		R^2	0.38*			0.51*									
	Positive Symptoms	partial *r*	0.10†	0.00	0.31*	0.09†	-0.01	0.07	0.06	0.00	0.10†	0.15*	0.03	-0.02	0.13*
		R^2	0.11*			0.18*									
	Addictions	partial *r*	0.12°	-0.13°	0.26*	0.13°	-0.12°	0.14*	0.15*	-0.02	0.07	-0.06	0.06	-0.03	-0.05
		R^2	0.11*			0.13*									
	Cognitive Impairment	partial *r*	-0.05	0.14*	0.50*	0.00	0.07	0.20*	0.15*	0.09†	0.49*	-0.02	-0.07	0.14*	-0.01
		R^2	0.25*			0.50*									

GFQ-58 – The General Functioning Questionnaire, WHOQOL-BREF – The WHO's Quality of Life Questionnaire - Short Version, CAS-1 – Cognitive-attentional Syndrome Questionnaire, RRS-B/R – Ruminative Response Scale, Brooding and Reflection subscales respectively, MCQ-1 – Metacognitions Questionnaire – Short Version, Cognitive Confidence subscale, MCQ-2 – Positive Beliefs subscale, MCQ-3 – Cognitive Self-consciousness subscale, MCQ-4 – Uncontrollability and Danger subscale, MCQ-5 – Need to Control Thoughts subscale, * $p \leq 0.001$, ° $p \leq 0.01$, † $p \leq 0.05$.

metacognitive beliefs. In both steps and for all models, the total scores of the GFQ-58 and WHOQOL-BREF as well as their subscales were significant (all p's < 0.001), the percent variance predicted by each model is presented in the R^2 columns in Table 3.

3.4. Conclusions

The results obtained indicate the satisfactory validity and reliability of the CAS-1. They also show that CAS symptoms are connected with various kinds of psychopathology symptoms and that these associations still hold when controlling for other measures of elements of CAS (rumination and metacognitive beliefs), which indicates that the CAS-1 has some unique properties. Regression models (created to show the ability of the CAS-1 to explain the variance of general psychopathology, various psychopathology symptoms, and quality of life when controlling for rumination and metacognitive beliefs) indicate that the CAS-1 is partially correlated with other measures of CAS and also possesses a unique ability to predict a significant amount of the variance of psychopathology and quality of life. It is worth noting that one of the most important popular tools for explaining CAS symptoms, apart from the CAS-1, is the RRS "Brooding" subscale. Also, different sets of metacognitive beliefs seem to play roles in explaining the variability of different types of symptoms. Therefore it may be concluded that assessment of CAS levels could be enhanced by combining different CAS measuring tools which would ensure that a larger percentage of the variance would be explained, thus ensuring the smallest measurement error possible.

4. Study 3

4.1. Procedure and sample characteristics

This study was conducted before an fMRI study in the Laboratory of Brain Imaging of the Institute of Experimental Biology of the Polish Academy of Sciences. Participants who took part in both parts of the study (diagnosis + fMRI) were given about 50 EUR in return. From participants of Study 1 ($N = 1225$), two extreme groups were selected, each with 134 participants. As the results of Study 2 suggest that combining tools which measure aspects of CAS predicts a greater amount of variance in psychopathology symptoms, a combination of measures was used in forming the two groups. The criteria for inclusion were obtaining scores above the 66th percentile or below the 33rd percentile on all of the following measures: the CAS-1, the "Brooding" subscale of the RRS (as this aspect of rumination is most prominently connected to emotional disorder) [cf. 37], and the "Need for Control" and "Uncontrollability and Danger" subscales from the MCQ-30, as these aspects of metacognitive beliefs are most prominently connected to levels of anxiety and depression [cf. 25,32,38,39]. Participants were invited to the study in random order and affiliation to groups was blinded. In the end, 98 participants took part in the present study: 44 from the High-CAS (HCAS) group and 54 from the Low-CAS (LCAS) group. Participants were first interviewed with SCID-I and were then asked to fill-in questionnaires. The study took about 2 h to complete.

4.2. Measures

In this study, the following measures presented in previous sections were used: the CAS-1, the RSS ($\alpha = 0.96$), and the MCQ-30 ($\alpha = 0.93$). Other measures were also used, which are described in detail below.

4.2.1. Structured clinical interview for DSM-IV-TR (SCID-I)

The SCID-I is a tool for the assessment of past and current psychiatric diagnoses but is limited to Axis I disorders – psychological disorders and mental illnesses, but not personality and developmental disorders [40]. It is based on DSM-IV-TR criteria [41]. This interview was administered by a trained clinical psychologist and psychotherapist (MD) with the use of the B/C module, as any psychotic symptoms were an exclusion criterion. The Polish adaptation of SCID-I (research version) was used [42].

4.2.2. Symptom checklist 27 plus (SCL-27-plus)

This is a checklist-type questionnaire that measures depressive, vegetative, agoraphobic, social phobia, and pain symptoms [43], and allows the calculation of a general symptoms index (GSI). The results on each scale can range from 0 to 20, where higher scores indicate higher levels of a given symptom. In this study, the Polish adaptation of the questionnaire was used [44], and it had an excellent internal consistency of $\alpha = 0.93$.

4.3. Results of study 3

In this study, the CAS-1 had an internal consistency of $\alpha = 0.91$. In general, the groups did not differ in demographic measures, except that the HCAS group had more females ($\chi^2 = 7.81$, $p = 0.005$; Cramér's $phi = 0.29$). There were significant differences between HCAS and LCAS groups in symptoms reported on the CAS-1 ($U = 73.5$, $p < 0.001$; Cohen's $d = 2.7$, d CI 95% = 2.15–3.25), RRS Brooding ($U = 117$, $p < 0.001$; Cohen's $d = 2.35$, d CI 95% = 1.84–2.87), MCQ-30 Uncontrollability and Danger ($U = 105.5$, $p < 0.001$; Cohen's $d = 2.41$, d CI 95% = 1.89–2.93), MCQ-30 Need to Control Thoughts ($U = 161$, $p < 0.001$; Cohen's $d = 2.20$, d CI 95% = 1.70–2.70), as well as SCL-27-plus GSI ($U = 148$, $p < 0.001$; Cohen's $d = 2.14$, d CI 95% = 1.65–2.64). Thus, the HCAS group scored significantly higher, on average, on all measures than did the LCAS group.

Analyses of SCID-I results revealed that Axis I disorders occurred significantly more often in the HCAS group. A lifetime diagnosis was established in 31 (70%) participants in the HCAS group in comparison to 6 (11%) in the LCAS group ($\chi 2 = 36.33$, $df = 1$, $p < 0.001$, Cramér's $V = 0.61$). A current diagnosis was established in 18 (41%) HCAS participants in comparison to 3 (6%) LCAS participants ($\chi 2 = 18.00$, $df = 1$, $p < 0.001$, Cramér's $V = 0.43$). Relative risk for lifetime diagnosis in the HCAS group was RR = 6.34 (CI 95% = 2.91–13.80) and for current diagnosis was RR = 7.36 (CI 95% = 2.32–23.39).

Current diagnoses in the HCAS group were as follows: 9 (50% of the sample) had anxiety disorders (i.e. GAD, social phobia, specific phobia), 4 (22%) had mood disorders (i.e. MDD, dysthymic disorder), 3 (17%) had PTSD comorbid with another Axis I disorder, and 2 (11%) had other disorders. Current diagnoses in the LCAS group were: 1 had PTSD, 1 had an anxiety disorder NOS, and 1 alcohol abuse disorder. Lifetime diagnoses in the HCAS group were as follows: 8 (26%) had anxiety disorders, 4 (13%) had mood disorders, 7 (23%) had comorbid anxiety and mood disorders, 5 (16%) had PTSD and anxiety and/or mood disorders, and the remaining 6 (19%) fulfilled criteria for other disorders. Lifetime diagnoses in the LCAS group were: 2 (33%) anxiety disorder NOS, and 4 other: 1 MDD comorbid with another Axis I disorder, 1 PTSD, 1 minor depressive disorder, and 1 alcohol abuse disorder.

Inclusion in the HCAS and LCAS groups on the basis of questionnaire results in the context of the presence of a lifetime diagnosis had sensitivity of 70% (CI 95% = 55%–83%) and specificity of 89% (CI 95% = 77%–96%). The positive predictive value was 84% (CI 95% = 70%–92%), the negative predictive value was 79% (CI 95% = 70%–85%), while the overall accuracy (sum of true positives and negatives divided by all results) of selection based on questionnaires was 81% (CI 95% = 71%–88%).

4.4. Conclusions

The results obtained indicate satisfactory reliability of the CAS-1 and satisfactory validity of a combination of the CAS-1, the "Brooding" subscale from the RRS, and two subscales from the MCQ-30. These measuring tools have satisfactory overall accuracy in detecting psychological disorders in a sample of people not currently undergoing psychiatric treatment. High levels of CAS are mostly connected to mood and anxiety

disorders and PTSD diagnoses. High levels of CAS symptoms are also connected to greater levels of psychopathology and pain symptoms.

5. General discussion

The aim of the presented studies was to explore the psychometric qualities of the CAS-1. The first study explored the validity and reliability of the CAS-1, its factor structure, and age and gender differences across a large community sample. The validity of the CAS-1 was explored through its relationships with metacognition and rumination questionnaires. The second study explored the validity of the CAS-1 through its relationships with a general functioning and psychopathology questionnaire and a quality of life questionnaire. The reliability of the CAS-1 was also explored. This study also allowed the identification of what amount of variance of psychopathology symptoms is explained by the CAS-1 when controlling for measures of metacognitive beliefs and rumination. The third study aimed to explore the predictive validity of CAS as a theoretical construct by ascertaining diagnoses in people with high and low levels of CAS. In light of results from the second study, the authors decided to broaden the questionnaire-based selection to other measures of elements of CAS: rumination and metacognitive beliefs. Subgroups based on the results of the CAS-1, the RRS's "Brooding" subscale, and the MCQ-30's "Need to Control Thoughts" and "Uncontrollability and Danger" subscales were diagnosed with a SCID-I structured interview and participants' levels of psychopathology symptoms were measured with the SCL-27-plus questionnaire.

There were gender differences in the CAS-1 results. This may result from gender differences in perceived levels of stress – women tend to obtain higher results on such measures [45–47], which may indicate that women are more prone to CAS because of higher levels of stressful events or a greater tendency to perceive events as stressful. Women also use emotional and avoidance styles to cope with stress more often [47]. It is noteworthy that these styles may be identified as elements of CAS – rumination [18] or thought suppression [6]. In particular, studies show that women are more likely than men to use rumination [48]. Likely because of this tendency, random selection in study 3 yielded a greater number of women in the HCAS group.

Four different theory driven factorial models of the CAS-1 were tested. All models had acceptable fit indices but χ^2 and BIC values indicate that the 2- and 4- factor models are a better fit to the data than the others and that the 2-factor model is superior to the 4-factor model. This may be understood as an indication that CAS-1 items can be easily divided into measures of cognitive and behavioral strategies on one hand and metacognitive beliefs on the other hand. But it should also be taken into account that the CAS-1 has only two items regarding basic CAS cognitive activities: repetitive negative thinking and threat monitoring. It may be hypothesized that the 4-factor structure proposed by Wells [2] would be preferable in a measuring tool with a more comprehensive assessment of those aspects, if such tool were to be devised.

The correlation analyses in studies 1 and 2 are in line with Wells' theory [2] and previous research which used the CAS-1 [15–17]. CAS-1 results have a medium-strength relationship with the measures of metacognitive beliefs and rumination. This indicates the construct validity of the CAS-1. CAS-1 results are also correlated with medium strength with levels of psychopathology symptoms (partial $r = 0.67$), and quality of life (partial $r = -0.57$) and its psychological domain (partial $r = -0.57$). This serves as a concurrent validity indicator. CAS-1 results are associated with different types of symptoms, not just depressive (partial $r = 0.62$) and anxiety symptoms (partial $r = 0.63$), which are known to be primarily linked to CAS levels [15,16]. They are also linked with other types of psychopathology such as cognitive deficits (partial $r = 0.50$), manic symptoms (partial $r = 0.47$), psychotic symptoms (partial $r = 0.31$), sexual disorder symptoms (partial $r = 0.38$), sleep disturbances (partial $r = 0.42$) [cf. 17], and somatic disorders (partial $r = 0.45$). This indicates the transdiagnostic character of CAS. However, it is important to note that the strongest relationships between CAS scores and disorder symptoms are with symptoms of depression and anxiety. This leads to the hypothesis that CAS is not only a key factor in the development of emotional disorders, which is in line with Wells' theory [2], but that it also may be a moderating factor in relationships between levels of psychopathology and subjective distress related to symptoms. It also may be hypothesized that levels of CAS are a moderating factor for relationships of mechanisms or risk factors of mental illnesses with subjectively rated levels of psychopathology symptoms. This would be associated with the high levels of comorbidity of various mental disorders, especially when anxiety or mood disorders are part of a diagnosis [49]. These hypotheses remain to be tested in further studies.

Most of these associations (apart from the Positive Symptoms subscale) remain with diminished strength after introducing other CAS variables (RRS and MCQ-30 subscales) to the regression models. More complex models explain a greater percentage of the variance of psychopathology symptoms and quality of life; the role of the CAS-1 in these models is smaller but CAS-1 scores are still significant predictors of the response variables, even when taking RRS and MCQ-30 scores into account. This may indicate some unique component of the CAS-1 in relation to these two measuring tools, which have been previously used to assess levels of CAS [10,12,13]. However, the creator of the CAS-1 [2] states that this measure is mostly for clinical use and for rare cases when it is not known which tool for the assessment of disorder-specific CAS symptoms is of use. This may indicate that devising a thorough CAS measure for use in scientific and clinical studies is appropriate. Such a measure should take into account all CAS components – worry, rumination, threat-sensitivity (internal and external), and, most strongly connected to emotional disorders metacognitive beliefs. Such a measure was simulated in the third study with the use of a combination of CAS-related measures.

The overall accuracy of the questionnaire-based diagnosis had an acceptable value of 71%–88%. There is medium probability of being diagnosed with a psychological disorder when in the HCAS group, and high probability of not receiving such a diagnosis when in the LCAS group. It should be noted that these values are considered acceptable because of the highly pre-selected sample. Potential participants who were undergoing any kind of psychiatric treatment or were generally unfit for participation in an fMRI were not included in studies 1 and 3. Bearing in mind that the sample explored in study 3 consisted of individuals who were by their own declaration "fit for the study", the obtained accuracy may be considered acceptable and serve as proof of the validity of a CAS diagnosis based on questionnaires and of the questionnaires' ability to distinguish between people with current and past psychological disorders as well as those who do not have a disorder.

As with all research, these studies have limitations. Concerning the samples: the sample in study 1 was supposed to mirror the population of Warsaw, instead it contained slightly more women and was better educated than the population. Study 2 was also not balanced in terms of gender and education – the participants were mostly women and people with higher education. Study 3, which consisted of subsamples from study 1, was pre-selected in terms of excluding participants who were undergoing psychiatric treatment and unsuitable for an fMRI study. These exclusion criteria do not allow this sample to be considered a community one and diminishes the ecological validity of the study. It may be hypothesized that in a group of high-CAS individuals there would be a higher percent of people with psychiatric disorders and illnesses who were unable to participate in this study due to undergoing some kind of treatment. It may also be hypothesized that the group of people with severe levels of CAS greatly overlapped with the group of people with severe psychological disorders who are thus unable or unwilling to participate in any kind of scientific study. For example, people with agoraphobia would not want to travel to an unknown location, people with claustrophobia would not want to partake in an fMRI study, etc. On the other hand, it could perhaps be suggested that people with some notion of their psychological disturbances were more prone

to participate in the study with the motivation of "checking themselves" and obtaining a psychological diagnosis free of charge.

6. Conclusions

The main conclusions of the studies discussed are as follows:

1. The CAS-1 has satisfactory reliability and validity.
2. Two and four factor structures of the CAS-1 were confirmed. The two-factor model had the best fit to the data in the large sample examined and in comparison to other proposed factor structures.
3. CAS may be perceived as a vulnerability factor for the development and continuance of various psychopathological symptoms.
4. High levels of CAS are connected with the occurrence of mood and anxiety disorders and PTSD.
5. The CAS-1 was devised for clinical purposes and, thanks to its brevity, may be useful in such a setting. For research purposes it would be helpful to devise a more extensive measure of CAS.
6. A combination of items from the worry, rumination, and metacognitive beliefs questionnaires with items concerning behavioral aspects of CAS could serve as such a measure.

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References

[1] Wells A. Emotional disorders and metacognition: innovative cognitive therapy. John Wiley & Sons; 2002.
[2] Wells A. Metacognitive therapy for anxiety and depression. New York: Guilford press; 2009.
[3] Wells A. Cognitive therapy of anxiety disorders: A practice manual and conceptual guide. John Wiley & Sons; 2013.
[4] Wells A, Matthews G. Modelling cognition in emotional disorder: the S-REF model. Behav Res Ther 1996;34(11):881–8.
[5] Borkovec TD, Shadick RN, Hopkins M. The nature of normal and pathological worry. In: Rapee RM, Barlow DH, editors. Chronic anxiety: generalized anxiety disorder and mixed anxiety-depression. New York: Guilford Press; 1991.
[6] Wegner DM, Zanakos S. Chronic thought suppression. J Pers 1994;62(4):615–40.
[7] Nolen-Hoeksema S. The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. J Abnorm Psychol 2000;109(3):504.
[8] Borkovec TD, Alcaine O, Behar E. Avoidance theory of worry and generalized anxiety disorder. In: Heimberg RG, Turk CL, Mennin DS, editors. Generalized anxiety disorder: advances in research and practice. New York: Guilford Press; 2004.
[9] Wells A, Carter K. Preliminary tests of a cognitive model of generalized anxiety disorder. Behav Res Ther 1999;37(6):585–94.
[10] Wells A, Carter K. Further tests of a cognitive model of generalized anxiety disorder: metacognitions and worry in GAD, panic disorder, social phobia, depression, and nonpatients. Behav Ther 2001;32(1):85–102.
[11] Papageorgiou C, Wells A. Metacognitive beliefs about rumination in recurrent major depression. Cogn Behav Pract 2001;8(2):160–4.
[12] Papageorgiou C, Wells A. An empirical test of a clinical metacognitive model of rumination and depression. Cogn Ther Res 2003;27(3):261–73.
[13] Papageorgiou C, Wells A. A prospective test of the clinical metacognitive model of rumination and depression. Int J Cogn Ther 2009;2(2):123–31.
[14] Sica C, Steketee G, Ghisi M, Chiri LR, Franceschini S. Metacognitive beliefs and strategies predict worry, obsessive–compulsive symptoms and coping styles: a preliminary prospective study on an Italian non-clinical sample. Clin Psychol Psychother 2007;14(4):258–68.
[15] Fergus TA, Bardeen JR, Orcutt HK. Attentional control moderates the relationship between activation of the cognitive attentional syndrome and symptoms of psychopathology. Personal Individ Differ 2012;53(3):213–7.
[16] Fergus TA, Valentiner DP, McGrath PB, Gier-Lonsway S, Jencius S. The cognitive attentional syndrome: examining relations with mood and anxiety symptoms and distinctiveness from psychological inflexibility in a clinical sample. Psychiatry Res 2013;210(1):215–9.
[17] Fergus TA, Scullin MK. The cognitive attentional syndrome is associated with sleep difficulties in a community sample. Behav Sleep Med 2017;15(5):410–20.
[18] Nolen-Hoeksema S. Gender differences in depression. Curr Dir Psychol Sci 2001;10(5):173–6.
[19] McLean CP, Asnaani A, Litz BT, Hofmann SG. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. J Psychiatr Res 2011;45(8):1027–35.
[20] Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatr 1994;51(1):8–19.
[21] Spada MM, Wells A. Metacognitions about alcohol use in problem drinkers. Clin Psychol Psychother 2006;13(2):138–43.
[22] Spada MM, Wells A. Metacognitive beliefs about alcohol use: development and validation of two self-report scales. Addict Behav 2008;33(4):515–27.
[23] Kiejna A, Piotrowski P, Adamowski T, Moskalewicz J, Wciórka J, Stokwiszewski J, et al. The prevalence of common mental disorders in the population of adult poles by sex and age structure – an EZOP Poland study. Psychiatr Pol 2015;49(1).
[24] Wells A, Matthews G. Attention and emotion: A clinical perspective. Hove. UK: Lawrence Erlbaum; 1994.
[25] Wells A, Cartwright-Hatton S. A short form of the metacognitions questionnaire: properties of the MCQ-30. Behav Res Ther 2004;42(4):385–96.
[26] Hunsley J. Introduction to the special section on incremental validity and utility in clinical assessment. Psychol Asses 2003;15(4):443.
[27] Central Statistical Office. Demographic yearbook of Poland. http://stat.gov.pl/obszary-tematyczne/roczniki-statystyczne/roczniki-statystyczne/rocznik-demograficzny-2014,3,8.html; 2014. [accessed 11.07.2017].
[28] Central Statistical Office. Population in Poland. Size and structure by territorial division. http://stat.gov.pl/obszary-tematyczne/ludnosc/ludnosc/ludnosc-stan-i-struktura-oraz-ruch-naturalny-w-przekroju-terytorialnym-stanu-w-dniu-30-06-2016-r-,6,20.html; 2016. [accessed 11.07.2017].
[29] Nolen-Hoeksema S, Morrow J. A prospective study of depression and posttraumatic stress symptoms after a natural disaster: the 1989 Loma Prieta earthquake. J Pers Soc Psychol 1991;61(1):115.
[30] Treynor W, Gonzalez R, Nolen-Hoeksema S. Rumination reconsidered: a psychometric analysis. Cogn Ther Res 2003;27(3):247–59.
[31] Kornacka M, Buczny J, Layton RL. Assessing repetitive negative thinking using categorical and transdiagnostic approaches: a comparison and validation of three polish language adaptations of self-report questionnaires. Front Psychol 2016;7:322.
[32] Dragan M, Dragan WŁ. Psychometric properties of the Polish version of the metacognitions questionnaire-30. Psychiatr Pol 2011;45(4):545–53.
[33] Kass RE, Raftery AE. Bayes factors. J Am Stat Assoc 1995;90(430):773–95.
[34] Styła R, Kowalski J. Psychometric properties of the General Functioning Questionnaire (GFQ-58) used for screening for symptoms of psychopathology and overall level of functioning. Psychiatr Pol 2019 (in press).
[35] WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychol Med 1998;28(3):551–8.
[36] Jaracz K, Kalfoss M, Górna K, Bączyk G. Quality of life in polish respondents: psychometric properties of the Polish WHOQOL–Bref. Scand J Caring Sci 2006;20(3):251–60.
[37] Olatunji BO, Naragon-Gainey K, Wolitzky-Taylor KB. Specificity of rumination in anxiety and depression: a multimodal meta-analysis. Clin Psychol Sci Pract 2013;20(3):225–57.
[38] Spada MM, Mohiyeddini C, Wells A. Measuring metacognitions associated with emotional distress: factor structure and predictive validity of the metacognitions questionnaire 30. Pers Individ Differ 2008;45(3):238–42.
[39] Sarisoy G, Pazvantoğlu O, Özturan DD, Ay ND, Yilman T, Mor S, et al. Metacognitive beliefs in unipolar and bipolar depression: a comparative study. Nord J Psychiatry 2014;68(4):275–81.
[40] First MB, Gibbon M, Spitzer RL, Williams JBW. SCID-I-TR: structured clinical interview for DSM-IV-TR disorders. New York: Biometrics Research; 2001.
[41] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., Text Revision; 2000 (Washington, DC).
[42] Popiel, A., Pragłowska, E., Zawadzki, B. (Polish version editors), 2014. Ustrukturalizowany wywiad kliniczny do badania zaburzeń z osi I DSM-IV-TR. Warszawa: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.
[43] Hardt J. The symptom checklist-27-plus (SCL-27-plus): a modern conceptualization of a traditional screening instrument. GMS Psycho-Social-Medicine 2008;5.
[44] Kuncewicz D, Dragan M, Hardt J. Validation of the polish version of the symptom checklist-27-plus questionnaire. Psychiatr Pol 2014;48(2):345–58.
[45] Turner RJ, Wheaton B, Lloyd DA. The epidemiology of social stress. Am Sociol Rev 1995:104–25.
[46] Almeida DM, Kessler RC. Everyday stressors and gender differences in daily distress. J Pers Soc Psychol 1998;75(3):670.
[47] Matud MP. Gender differences in stress and coping styles. Personal Individ Differ 2004;37(7):1401–15.
[48] Kwon H, Yoon KL, Joormann J, Kwon JH. Cultural and gender differences in emotion regulation: relation to depression. Cogn Emot 2013;27(5):769–82.
[49] Hasin DS, Grant BF. The national epidemiologic survey on alcohol and related conditions (NESARC) waves 1 and 2: review and summary of findings. Soc Psychiatry Psychiatr Epidemiol 2015;50(11):1609–40.

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Neural Correlates of Cognitive-Attentional Syndrome: An fMRI Study on Repetitive Negative Thinking Induction and Resting State Functional Connectivity

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Aim: Cognitive-attentional syndrome (CAS) is the main factor underlying depressive and anxiety disorders in the metacognitive approach to psychopathology and psychotherapy. This study explore neural correlates of this syndrome during induced negative thinking, abstract thinking, and resting states.

Methods: n = 25 people with high levels of CAS and n = 33 people with low levels of CAS were chosen from a population-based sample (N = 1225). These groups filled-in a series of measures of CAS, negative affect, and psychopathology; they also underwent a modified rumination induction procedure and a resting state fMRI session. Resonance imaging data were analyzed using static general linear model and functional connectivity approaches.

Results: The two groups differed with large effect sizes on all used measures of CAS, negative affect, and psychopathology. We did not find any group differences in general linear model analyses. Functional connectivity analyses showed that high levels of CAS were related to disrupted patterns of connectivity within and between various brain networks: the default mode network, the salience network, and the central executive network.

Conclusion: We showed that low- and high-CAS groups differed in functional connectivity during induced negative and abstract thinking and also in resting state fMRI. Overall, our results suggest that people with high levels of CAS tend to have disrupted neural processing related to self-referential processing, task-oriented processing, and emotional processing.

Keywords: repetitive negative thinking, cognitive-attentional syndrome, rumination, resting state, fMRI, neural correlates

INTRODUCTION

Cognitive-attentional syndrome (CAS) is a key construct in Wells' metacognitive theory of emotional disorders (Wells and Matthews, 1994; Wells, 2009). In the Self-Regulatory Executive Function (S-REF) model, CAS is a set of psychological processes that includes repetitive negative thinking (worry and rumination), threat monitoring, and associated unhelpful behavioral and cognitive strategies; it is derived from metacognitive beliefs, either positive (e.g., "If I ruminate I will understand my situation") or negative (e.g., "I cannot control my ruminative thoughts"). While moments of negative self-appraisal are relatively brief in most people, the prolonged occurrence of negative emotions and negative self-appraisal in some people is due to recurring activation of CAS. This specific style of responding to negative thoughts is considered a transdiagnostic factor which underlies emotional disorders. Many studies have confirmed the relationship of CAS with emotional distress as well as symptoms of mood and anxiety disorders (Fergus et al., 2012, 2013). According to the metacognitive model, CAS is a prominent factor in the development of mood disorders, e.g., major depressive disorder (MDD; Papageorgiou and Wells, 2001, 2003, 2009; Wells, 2009), anxiety disorders, e.g., generalized anxiety disorder (GAD; Wells, 1999, 2005, 2007, 2009), post-traumatic stress disorder (PTSD; Wells and Sembi, 2004; Wells, 2009; Bennett and Wells, 2010), and obsessive-compulsive disorder (OCD; Fisher and Wells, 2005; Myers et al., 2009a,b; Wells, 2009; Solem et al., 2010).

A fundamental element of CAS is a pattern of negative, pervasive, and recurring thoughts. Rumination is associated with decreased attentional resources (Donaldson et al., 2007; Koster et al., 2011), the occurrence of negative emotions, and difficulties with problem solving (Nolen-Hoeksema et al., 2008). A ruminative thinking style is most often associated with mood disorders, as it is a risk factor for the development of depression (Nolen-Hoeksema et al., 2008) and is generally associated with dysphoric and depressive mood (Mor and Winquist, 2002). However, rumination is not only present in mood disorders – it also plays a prominent role in the symptomatology of other emotional and psychiatric disorders, such as anxiety or eating disorders (Olatunji et al., 2013). Pathological worry, another form of extended thinking, is considered a key feature of GAD; however, many researchers have shown that it also occurs in other types of emotional disorders (e.g., Starcevic et al., 2007; Spinhoven et al., 2015).

To date, there have been no studies on brain functioning in people with high levels of CAS – i.e., elevated levels of CAS-related symptomatology: repetitive negative thinking, attention to threats, unhelpful coping behaviors, and maladaptive metacognitive beliefs. There are, however, some studies using functional magnetic resonance imaging (fMRI) methods in which induction of core aspects of CAS – rumination (state rumination rather than trait rumination; Cooney et al., 2010; Berman et al., 2014; Burkhouse et al., 2017) or worry (Paulesu et al., 2010) – has been employed. The first two of the aforementioned studies on rumination induction compared depressed participants to healthy controls, while the third compared adolescents with remitted MDD to healthy controls. The Rumination Induction task used in an fMRI setting by Cooney et al. (2010) consisted of alternating blocks of ruminative, concrete, and abstract sentences which participants were asked to think about (e.g., "think about the expectations people have for you"). In this procedure, ruminative sentences, in comparison to concrete/abstract sentences, were associated with altered activity in brain regions involved in emotion processing and regulation in depressed patients: the dorsolateral prefrontal cortices, cingulate cortices, amygdalae, and parahippocampi (Cooney et al., 2010). Another study compared resting state functional connectivity with functional connectivity during negative mood induction using personalized cues created by ruminating on negative autobiographical events (e.g., "Please recall a specific time when you were very embarrassed"; Berman et al., 2014). This study showed that depressed patients had stronger connections within brain regions belonging to the default mode network (DMN), like the cingulate cortex. It was suggested that these results may be understood as difficulty in down-regulating self-oriented emotional and cognitive processing after rumination induction (Berman et al., 2014). A fourth study (Burkhouse et al., 2017) found that rumination induction with prior negative mood induction (e.g., "Remember when you failed badly at something") elicits stronger neural activations in regions involved in the DMN and emotion processing in remitted MDD adolescents. A study by Paulesu et al. (2010) explored differences in worrying between patients with GAD and healthy controls. Sentences which induce worrying (e.g., "Mull over what worries you about your future") were related to activation in the anterior cingulate and dorsal medial prefrontal cortex in the GAD group.

Several recent meta-analyses on neuronal functioning in people with depression (Hamilton et al., 2012; Palmer et al., 2015), specific phobias (Ipser et al., 2013), and PTSD (Simmons and Matthews, 2012) show, in general, that emotional disorders are most prominently connected to the dysregulation of subcortical brain areas involved in emotion processing, i.e., the amygdalae and hippocampi, as well as the striatum. This dysregulation is interpreted as the overdeveloped salience of threatening or saddening stimuli. Also, several cortical regions are involved in this type of processing, like the insulae and dorsolateral prefrontal cortices. Studies on repetitive negative thinking induction and large meta-analyses on emotional disorders have found that people experiencing mood and anxiety disorders exhibit dysregulation of the default mode, salience, and executive networks. Overall, people with emotional disorders demonstrate a pattern of disrupted neural processing in the areas of self-referential, task-oriented, and emotional processing (Hamilton et al., 2012; Simmons and Matthews, 2012; Ipser et al., 2013; Palmer et al., 2015).

In the current study, we aimed to explore differences in neural functioning between people with high and low levels of CAS symptoms. Given that there are no previous studies on the neural correlates of CAS, we decided to base our hypotheses on available work on repetitive negative thinking induction and meta-analytical results regarding emotional disorders which, according to metacognitive theory, are undergirded by CAS. We hypothesized that people with high levels of CAS symptoms

will show similar patterns of cortical activations to those found in studies on neural correlates of depressive and anxiety disorders, as described above. To test these hypotheses, we employed a modified Rumination Induction procedure and resting state functional magnetic resonance imaging (rsfMRI). We expected that differences in neural activation in people with high levels of CAS symptoms (HCAS) would be comparable to the patterns of activation reported by Cooney et al. (2010) in depressed patients, with greater neural activity in the amygdalae, hippocampi, and cingulate and dorsolateral cortices in the rumination condition as compared to the abstract condition. We also hypothesized that the cortical regions associated with rumination and which show aberrant activity in emotional disorders will show different patterns of functional connectivity in the HCAS group in comparison to the group with low levels of CAS symptoms (LCAS). We expected to find disrupted patterns of connectivity within and between several neural networks: the DMN, the salience network, and the central executive network (CEN).

MATERIALS AND METHODS

Procedure and Sample Selection

Participation in the study was voluntary and participants gave their informed consent. The study was approved by the Research Ethics Committee at the Faculty of Psychology, University of Warsaw. The study was conducted in two stages. The first stage took place through an Internet survey panel and was conducted by an external company. A large sample was gathered for the purpose of an fMRI study, so there were standard strict exclusion criteria related to the fMRI procedure (left-handedness, metal objects within the body, irremovable piercings, etc.) as well as any history of neurological or serious mental disorders or substance abuse disorders. Participants were also required to live in the Warsaw area to ensure their ability to participate in the second stage of the study. A total of 1,225 participants were eligible and completed the first stage of the study. Participants were selected based on quotas mirroring the population of Warsaw (Central Statistical Office, 2017) in terms of sex, age, and education. **Figure 1** depicts the selection procedure from the first to the final stage of the study.

From the first stage participants, two extreme groups were selected. As the results of previous studies (Kowalski and Dragan, 2019) have suggested that combining different measures of aspects of CAS is best for predicting levels of psychopathology, several measures were used in forming the two groups. The cut-off criterion was a score above the 66th percentile or below the 33rd percentile of the sum of results on the following measures: the CAS-1 questionnaire, the Brooding subscale of the RRS (as this aspect of rumination is most robustly associated with depressive and anxiety disorders, cf. Olatunji et al., 2013), and the Need to Control Thoughts as well as the Uncontrollability and Danger subscales from the MCQ-30, as these aspects of metacognitive beliefs are most prominently connected to levels of anxiety and depression (cf. Wells and Cartwright-Hatton, 2004; Spada et al., 2008; Dragan and Dragan, 2011; Sarisoy et al., 2014). Finally two extreme groups, each consisting of 134 subjects, were formed.

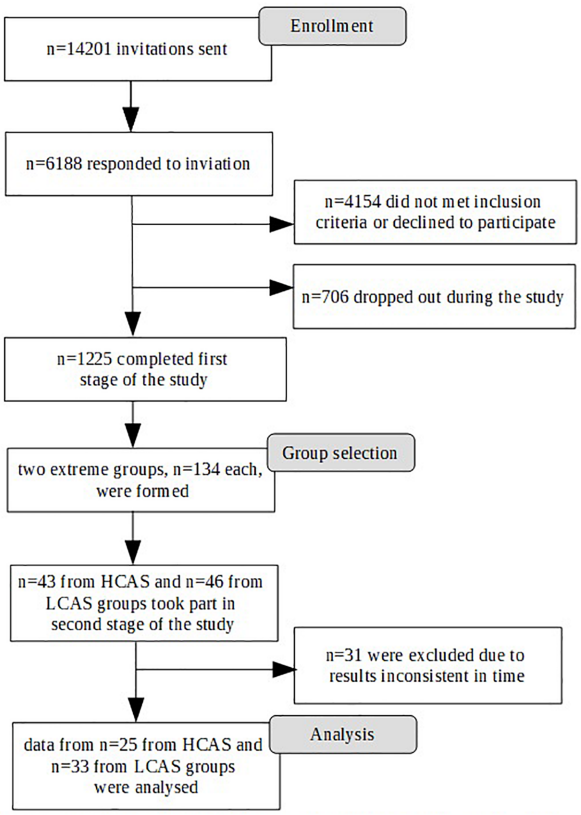

FIGURE 1 | Consort flow-chart of enrollment and samples selection for the study.

The second stage of the study took part in the Laboratory of Brain Imaging, Neurobiology Center, Nencki Institute of Experimental Biology, Polish Academy of Sciences. Participants were invited to the laboratory in a random order by a person from an external company. Researchers were blinded to the participants' group affiliation. A total of 89 participants took part in the study – 43 in the HCAS group and 46 in the LCAS group. Participants who underwent the whole fMRI procedure were given a sum of money equivalent to about 50 EUR.

The second stage of the study occurred 4–22 weeks after the first stage, depending on the timing of the participants' second stage appointment. Despite the acceptable time-stability of the questionnaire results between the first and second stages of the study (correlations of results at these two time points: CAS-1: $r = 0.83$, $p < 0.001$, RRS – Brooding: $r = 0.82$, $p < 0.001$, MCQ – Need to Control Thoughts: $r = 0.76$, $p < 0.001$, MCQ – Uncontrollability and Danger: $r = 0.82$, $p < 0.001$) some shift in individual results was observed. To ensure that both groups had extreme characteristics, participants had to have results above or below median on all four measures used in the study. As a result, 31 participants were excluded: 30 had mixed results and 1 "changed groups" as this participant had HCAS results

TABLE 1 | Group characteristics – demographic and clinical variables.

		HCAS (n = 25)	LCAS (n = 33)	t-Test	p-Value	Cohen's d (90% CI)
Sex		72% females	42% females	5.03*	0.025	0.30**
Age		30.40 (7.26)	33.48 (5.85)	−1.74	0.089	
CAS-1		75.90 (9.98)	23.88 (11.21)	18.33	< 0.001	4.90 (4.04–5.77)
RRS-brooding		15.72 (2.57)	7.09 (1.81)	14.30	< 0.001	3.88 (3.15–4.62)
MCQ-30	Need to control thoughts	16.64 (2.64)	7.67 (1.51)	15.19	< 0.001	4.17 (3.40–4.94)
	Uncontrollability and danger	19.28 (2.99)	8.70 (2.79)	13.87	< 0.001	3.66 (2.95–4.37)
SCL-27 plus	Depression	9.63 (4.32)	0.62 (1.04)	9.99	< 0.001	2.87 (2.25–3.48)
	Vegetative symptoms	8.28 (3.35)	3.88 (3.05)	5.22	< 0.001	1.37 (0.89–1.85)
	Agoraphobic symptoms	4.64 (2.91)	0.52 (1.06)	6.75	< 0.001	1.88 (1.36–2.4)
	Sociophobic symptoms	11.04 (2.47)	2.67 (2.17)	13.68	< 0.001	3.6 (2.90–4.30)
	Pain	9.72 (3.02)	5.90 (2.45)	5.30	< 0.001	1.39 (0.91–1.87)
	Total score	43.46 (9.69)	13.72 (7.06)	13.30	< 0.001	3.51 (2.82–4.20)

**Chi-squared test; **Cramer's Phi; CAS-1, Cognitive-Attentional Syndrome Questionnaire; RRS-brooding, Ruminative Response Scale - brooding subscale; MCQ-30, Metacognitions Questionnaire - Short Version; SCL-27 plus, Symptoms Checklist 27-plus.*

on the internet measures but LCAS results on the day of the fMRI scan. Ultimately, data from 58 participants (HCAS = 25, LCAS = 33) were analyzed and are presented in this paper. Group demographic characteristics are presented in **Table 1**. These groups were also clinically diagnosed with a SCID-I interview but full results are presented elsewhere (Kowalski and Dragan, 2019; Dragan and Kowalski, unpublished). A total of 45% of participants from the HCAS group and none from LCAS group met the diagnostic criteria for a current diagnosis of a psychological disorder. In the HCAS group, 12 participants were diagnosed according to DSM-IV-TR criteria with: MDD (1), dysthymic disorder (1), GAD (2), GAD comorbid with social phobia (1), GAD comorbid with social phobia and dysthymic disorder (1), PTSD comorbid with MDD (1), PTSD comorbid with social phobia (1), PTSD comorbid with binge eating (1), cyclothymic disorder comorbid with bulimia nervosa (1), depressive disorder NOS (1), and anxiety disorder NOS (1). All participants were treatment-naive and diagnosis-naive at the beginning of the study. The second stage of the procedure consisted of filling-in questionnaires (CAS-1, RRS, MCQ-30, SCL-27) followed by the MRI procedure, including: a T1-weighted structural scan, rsfMRI, and a Rumination Induction procedure. This MRI procedure lasted approximately 40 min in total and constituted a part of a larger MRI study. After the MRI procedure, participants filled-in PANAS and STAI questionnaires. A schematic representation of the procedure is displayed in **Figure 2**.

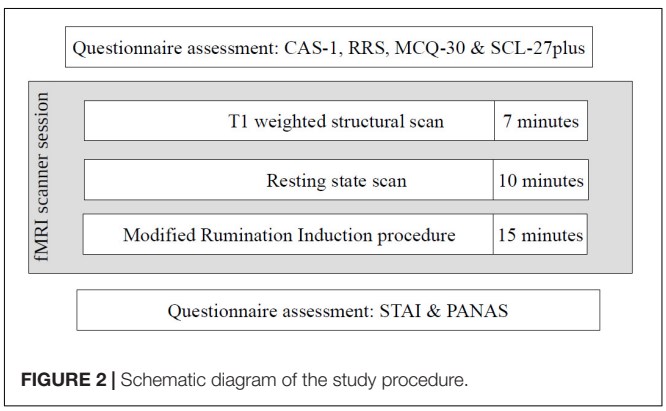

FIGURE 2 | Schematic diagram of the study procedure.

Measures and Materials

The Cognitive-Attentional Syndrome Questionnaire (CAS-1)

The CAS-1 questionnaire (Wells, 2009) consists of 16 items measuring aspects of CAS: worry/rumination, attention to threat, maladaptive behaviors, and metacognitive beliefs. The results of the questionnaire were calculated as in the paper by Fergus et al. (2012) – the last eight items were recalculated to range between 0 and 8 before summing them up. The total results range from 0 to 128, where a higher result indicates a greater level of CAS. The psychometric qualities of the Polish version of CAS-1 are presented elsewhere (Kowalski and Dragan, 2019). In the current study, CAS-1 had excellent internal consistency of Cronbach's $\alpha = 0.91$.

Ruminative Response Scale (RRS)

The 22-item Ruminative Response Scale focuses on one's responses to depressive mood: concentration on the self, symptoms, and the causes and consequences of depressive mood. A newer approach (Treynor et al., 2003) distinguishes two subscales: "Reflection" and "Brooding." Only the results of the latter are presented in this study. This subscale consists of five items with results ranging from 5 to 20, where a higher result indicates a greater tendency to respond to depressed mood with brooding. The Polish version of the RRS has generally good psychometric qualities (Kornacka et al., 2016). In the current study, the Brooding subscale had internal consistency of Cronbach's $\alpha = 0.88$.

Metacognitions Questionnaire – Short Version (MCQ-30)

The short version of the Metacognitions Questionnaire, developed by Wells and Cartwright-Hatton (2004), consists of five subscales and 30 items. It concerns metacognitive beliefs:

monitoring techniques, judgments, and beliefs about one's thoughts and cognitive abilities central to the metacognitive model of psychopathology. Two subscales are of interest in present study: the "Uncontrollability and Danger" scale explores the negative aspects of worry, e.g., "My worrying is dangerous for me" and the "Need to Control Thoughts" scale deals with beliefs about the negative consequences of not controlling one's thoughts, e.g., "Not being able to control my thoughts is a sign of weakness." The Polish version of this questionnaire exhibits good psychometric qualities and is considered equivalent to the English version (Dragan and Dragan, 2011). In this study, these two MCQ-30 subscales had good internal consistencies of $\alpha = 0.89$ and $\alpha = 0.84$, respectively.

Symptom Checklist 27 Plus (SCL-27-Plus)

This is a checklist-type questionnaire that measures depressive, vegetative, agoraphobic, sociophobic, and pain symptoms (Hardt, 2008), and it allows the calculation of a global severity index (GSI). The results on each scale can range from 0 to 20, where higher scores indicate higher levels of a given symptom. In this study, the Polish adaptation of the questionnaire was used (Kuncewicz et al., 2014) and it had an excellent internal consistency of Cronbach's $\alpha = 0.93$.

Positive and Negative Affect Schedule (PANAS)

This is a comprehensive measure of emotions with two distinct subscales of positive and negative affect (Watson et al., 1988). In this study, a Polish adaptation of the 30-item PANAS-state questionnaire, which has good psychometric qualities, was used (Brzozowski et al., 2010). In the current study, the internal consistencies of its subscales were $\alpha = 0.82$ and $\alpha = 0.80$, respectively.

State-Trait Anxiety Inventory (STAI)

A widely used measurement of anxiety and its cognitive and vegetative components (Spielberger et al., 1970). In this study, a Polish adaptation of the STAI-state questionnaire, which has good psychometric qualities, was used (Wrześniewski et al., 2002). In the current study, the internal consistency was Cronbach's $\alpha = 0.93$.

Resting State fMRI

The resting state procedure consisted of a fixation cross being shown for 10 min on the MRI display (cf. Birn et al., 2013; Patriat et al., 2013). Subjects were instructed to fix their gaze on the cross and to not move.

Modified Rumination Induction (RumInd-M) fMRI Task

During rumination induction, participants are asked to think about sentences that are designed to induce the process of rumination (Nolen-Hoeksema and Morrow, 1993). The sentences deal with themes of the reader's own emotions, appraisals, and experiences. In this task, we used the mix of stimuli used by Cooney et al. (2010; rumination induction) and by Paulesu et al. (2010; worry induction) to obtain a robust repetitive negative thinking effect in participants. We used the modified procedure from Cooney et al. (2010) with ruminative/worrying sentences (e.g., "Think about the opportunities you didn't take in your life," "Think about what worries you have about your health"; RUM), and abstract sentences (e.g., "Think about how a plant grows"; ABS) as a control condition (see **Appendix 1** for all stimuli used). Participants were asked to think about sentences presented on screen and to try to clear their minds when a cross appeared on screen. Each sentence was presented on screen for 30 s and sentences were separated by 10 s of a fixation cross. Four blocks of five sentences were presented in a non-consecutive order (RUM-ABS-RUM-ABS). After each block, participants assessed their sadness, anxiety, and engagement in thinking on a 1–5 Likert scale. Results from this task are the totals of the assessments from both blocks of the same type. The task lasted about 15 min. Two parallel versions of rumination induction were used. Versions did not differ on any of the results (all values of $p > 0.05$) and administration of the versions did not differ between HCAS and LCAS groups, $\chi^2 = 0.43$, $p = 0.51$.

Behavior Analysis

Internal consistency was calculated with Cronbach's α. Group differences were analyzed with Student's *t*-test for independent samples or χ^2 for nominal data, group differences were calculated to demonstrate effect sizes using Cohen's *d*. Data were analyzed with IBM SPSS 24, effect sizes were calculated using an online calculator[1].

MRI Data Acquisition and Analysis

Data were acquired using a 3T Siemens MAGNETOM Trio system (Siemens Medical Solutions) equipped with a 12-channel head coil: structural T1-weighted image (TR: 2,530 ms, TE: 3.32 ms, flip angle: 7°, voxel size: 1 × 1 × 1 mm, field of view: 256 mm, measurements: 1), rsfMRI (TR: 2,000 ms, TE: 28 ms, flip angle: 80°, voxel size: 3 × 3 × 3 mm, field of view: 216 mm, measurements: 200), and task fMRI (TR: 2,500 ms, TE: 28 ms, flip angle: 80°, voxel size: 3 × 3 × 3 mm, field of view: 216, measurements: 364). After the rsfMRI and rumination induction tasks, B0 inhomogeneity field maps were collected (TR: 400 ms, TE: 4.5 ms/6.96 ms, flip angle: 60°, voxel size: 3 × 3 × 3 mm, field of view: 216 mm, measurements: 1).

The DICOM series were converted to NIfTI and BIDS data formats with Horos Bids Output[2]. Spatial preprocessing was performed using Statistical Parametric Mapping (SPM12[3]). Functional images were corrected for distortions related to magnetic field inhomogeneity, corrected for motion by realignment to the first acquired image, slice-timed, normalized to the MNI space, and resliced to obtain a resolution of 2 × 2 × 2 mm, and smoothed with the 6 mm FWHM Gaussian kernel. Before normalization, structural images were coregistered to the mean functional image and segmented into separate tissues using the default tissue probability maps. Functional data were also analyzed with the Artifact Detection Toolbox (ART[4]). Any EPI which deviated from the previous one by 3SD, 1.6 mm, or

[1]https://www.psychometrica.de/effect_size.html
[2]https://github.com/mslw/horos-bids-output
[3]http://www.fil.ion.ucl.ac.uk/spm/
[4]https://www.nitrc.org/projects/artifact_detect

0.04 rad was considered an outlier and such EPIs were regressed out in the 1st level models. Averages of 4.12%, *SD* = 2.64%, of scans for the rumination induction task and of 4.74%, *SD* = 4.13%, of scans for rsfMRI were regressed out. Participants with more than 20% outliers were excluded from the analyses. Based on these criteria no participants were excluded. There were no differences between groups in the number of outliers in the rumination induction task ($t = 0.23$, $p = 0.82$) or in the resting state ($t = -1.76$, $p = 0.08$), there were also no differences in the number of outliers between RUM and ABS conditions ($t = 0.23$, $p = 0.82$). Functional data were high pass filtered (1,000 s for rumination induction and 128 s for rsfMRI), and fixation crosses in the rumination induction task were modeled as baseline. Data were analyzed as a flexible factorial model of group × condition activation and with a two sample *t*-test of RUM > ABS and ABS > RUM contrasts. A regressor with a mock variable for gender was added to the second level models. On a group level, a voxel-wise height threshold of $p < 0.05$ corrected for multiple comparisons using the family wise error (FWE) rate was employed for whole brain analyses. Thresholded fMRI maps and raw data are available to any researcher upon request.

Functional Connectivity Analyses

The CONN (ver. 18[5]) toolbox was used to perform functional connectivity analyses. First level SPM files and functional data for the resting state and rumination induction were imported into the software. Data were denoised with use of the respective T1-weighted scans, normalized to MNI-space, with eight regressors for WM and seven regressors for CSF, and with movement parameters obtained with the ART toolbox. The acceptance threshold for denoised signal voxel-to-voxel correlations was on average $r \leq 0.1$. Resting state connectivity was calculated as HRF modulated pairwise correlations with seed-to-voxel analyses with a regressor for gender. RumInd connectivity was calculated as HRF modulated pairwise regressions with seed-to-voxel analyses of the generalized psychophysiological interaction (gPPI; McLaren et al., 2012) of group (HCAS and LCAS) versus condition (RUM and ABS) interactions with a regressor for gender. To make things clearer, η^2, the effect size for the interaction analysis, was transformed into Cohen's *d* using an online calculator (see footnote 1). The threshold for significance was set at $p \leq 0.05$ with false discovery rate cluster correction (FDRc). Figures depicting the connectivity analyses were made with use of MRIcroGL[6].

Seed Definitions

ROIs (regions of interest) chosen for functional connectivity seeds were based on main effects of the RUM condition from the rumination induction task and analysis of meta-analytic literature on the neural correlates of emotional disorders (i.e., depression and anxiety), these being conceptually most similar to CAS activation. Spheres of $r = 6$ mm were created over the obtained peak activations or the coordinates of peak activations provided by other authors. The MarsBar toolbox[7] was used to create ROIs. Talairach coordinates from meta-analyses were converted to MNI coordinates with the mni2tal calculator[8]. Nine ROIs were extracted from the RUM > ABS contrast from the rumination induction task: left and right precunei [−4 −58 32, −8 −52 28 and 6 −52 26], middle cingulate cortex [0 −18 36], L-paracingulate gyrus [−6 52 8], L- and R-superior frontal gyri [−2 56 38 and 6 52 28] and L- and R-frontal poles [−4 62 24 and 4 56 10]. Task-based ROI labels were based on an Harvard–Oxford anatomical atlas. Nine ROIs were extracted from meta-analyses on depressive and anxiety disorders: sub-callosal gyrus [2 16 −12], R-anterior cingulate cortex [10 30 −4] (Depression; Palmer et al., 2015), L-insula [−41 −3 −14], R-dorsal anterior cingulate cortex [−2 32 21], R-dorsolateral prefrontal cortex [30 10 50], and L-dorsolateral prefrontal cortex [−23 25 46] (Depression; Hamilton et al., 2012), L-insula [−42 14 −1] (Social anxiety disorder; Ipser et al., 2013), R-anterior cingulate [5 28 18], and R-middle frontal gyrus [41 9 40] (PTSD; Simmons and Matthews, 2012). Literature-based ROI labels were based on nomenclature used by the authors of meta-analyses. Due to the long-block nature of the rumination induction task, we limited these analyses to cortical regions chosen as ROIs.

RESULTS

Behavioral Results

HCAS and LCAS groups differed strongly on all CAS measures (CAS-1, RRS-brooding, and MCQ-30 subscales) and all the subscales of SCL-27-plus used in this study. All differences were large in effect size with values of $d > 3.5$ for CAS measures and values of $d > 1.3$ for measures of psychopathology. There were more women in the HCAS group, for this reason, a mock variable for gender was added to the second levels of the fMRI and functional connectivity analyses. The groups also differed significantly with medium-to-large effect sizes on their assessments during rumination induction, both in RUM and ABS conditions as well as post-scan measurements of anxiety and negative emotions – for details see **Table 2**.

Neuroimaging Results

Significant neural activations in the whole sample for RUM > ABS and ABS > RUM contrasts are presented in **Figure 3** and **Table 3**. The RUM > ABS condition yielded activations in bilateral precunei, bilateral superior frontal cortices, bilateral frontal poles, and the middle cingulate cortex. The ABS > RUM condition yielded several cortical activations: bilateral middle temporal gyri, bilateral supramarginal gyri, L-precentral gyrus, R-middle and inferior frontal gyri, and bilateral frontal poles. We did not find any differences between groups in neuronal activity in contrasts between RUM and ABS conditions in the rumination induction task, in the flexible factorial model, or in the two sample *t*-test models.

[5]https://www.nitrc.org/projects/conn

[6]https://www.mccauslandcenter.sc.edu/mricrogl/

[7]http://marsbar.sourceforge.net/

[8]http://sprout022.sprout.yale.edu/mni2tal/mni2tal.html

TABLE 2 | Behavioral results of RumInd-M task and post-scan assessments.

		HCAS (n = 25)	LCAS (n = 33)	t-Test	p-Value	Cohen's d (90% CI)
Modified rumination induction	RUM-sadness	4.24 (1.64)	2.09 (0.39)	6.40	< 0.001	1.80 (1.29–2.32)
	RUM-anxiety	4.04 (2.07)	2.03 (0.18)	4.84	< 0.001	1.37 (0.89–1.85)
	RUM-engagement	8.56 (1.76)	8.28 (2.23)	0.51	0.611	
	ABS-sadness	2.84 (1.03)	2.00 (0.00)	4.07	< 0.001	1.15 (0.69–1.62)
	ABS-anxiety	3.12 (1.72)	2.03 (0.18)	3.16	0.004	0.89 (0.44–1.34)
	ABS-engagement	8.24 (1.96)	8.84 (1.59)	−1.28	0.205	
STAI-state		42.32 (11.26)	29.55 (4.64)	5.34	< 0.001	1.48 (1.00–1.97)
PANAS-negative emotions		27.56 (10.51)	16.21 (1.55)	5.35	< 0.001	1.51 (1.02–2.00)

RUM, ABS, conditions in RumInd-M task; STAI, State-Trait Anxiety Inventory - State Version; PANAS, Positive and Negative Affect Schedule.

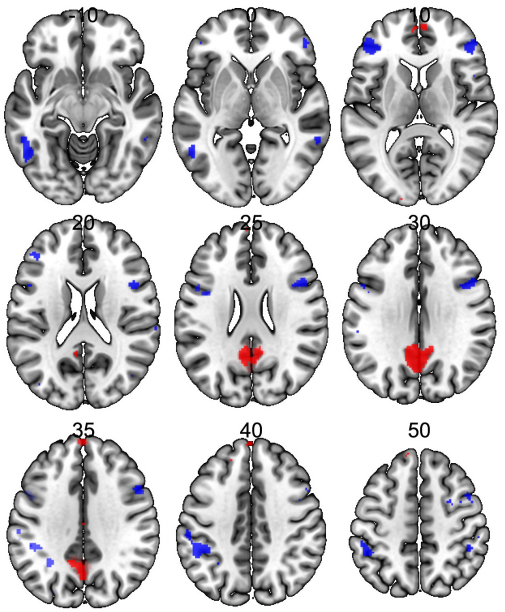

FIGURE 3 | Neural activations in the whole sample (both groups together) for RUM > ABS and ABS > RUM contrasts. Red clusters depict activations in the RUM > ABS contrast, blue clusters depict activations in the ABS > RUM contrast. For details, see **Table 3**.

TABLE 3 | Structure activations for both groups in RUM > ABS and ABS > RUM contrasts with FWE correction ($p \leq 0.05$).

Structure name	Cluster size	Peak Z-value	MNI coordinates [x y z]
RUM > ABS contrast			
L-Precuneus*	613	6.43	−4 −58 32
L-Precuneus*	613	6.30	−8 −52 28
R-Precuneus*	613	6.13	6 −52 26
L-Superior frontal gyrus	31	5.30	−2 56 38
	2	5.02	−18 40 38
R-Frontal pole	11	5.16	4 56 10
L-Paracingulate gyrus	26	5.08	−6 52 8
L-Frontal pole	7	5.03	−4 62 25
	4	4.90	−12 44 50
Middle cingulate cortex	2	4.76	0 −18 36
R-Superior frontal gyrus	1	4.83	6 52 28
ABS > RUM contrast			
L-Frontal pole	315	7.18	−46 40 12
R-Middle temporal gyrus	108	6.57	60 −56 −6
L-Middle temporal gyrus*	372	6.49	−54 −56 −6
L-Inferior temporal gyrus*	372	6.33	−50 −60 −14
L-Supramarginal gyrus	326	6.47	−50 −42 50
R-Frontal pole	179	6.22	48 38 4
R-Middle frontal gyrus*	219	5.76	50 14 34
R-Inferior frontal gyrus*	219	5.73	46 10 18
L-Middle frontal gyrus	33	5.43	−50 10 32
L-Superior parietal lobule	21	5.24	−30 −54 38
R-Middle frontal gyrus	80	5.20	40 4 58
R-Supramarginal gyrus	23	5.19	44 −40 50
L-Precentral gyrus	13	5.11	−40 2 24

*R, right hemisphere; L, left hemisphere; *one cluster containing parts of two structures.*

gPPI Results

Table 4 and **Figure 4** displays results of gPPI of group and condition interactions. The L-precuneus [−4 −58 32] showed increased connectivity with parts of the L-lateral occipital cortex and supramarginal gyrus in the HCAS group in the RUM condition in comparison to the LCAS group and decreased connectivity with bilateral parts of the precunei in the RUM condition in comparison to the LCAS group; opposite effects were observed in the ABS condition. The L-superior frontal gyrus showed decreased connectivity with parts of the L-superior parietal lobule and postcentral gyrus in the HCAS group in the ABS condition in comparison to the LCAS group and increased connectivity with the R-precuneus in this group in the ABS condition in comparison to LCAS group; opposite effects were seen in the RUM condition. Also, the L-precuneus [−8 −52 28] showed increased connectivity with bilateral frontal poles in the HCAS group in the RUM condition in comparison to the LCAS group and the opposite effect was found in the ABS condition. There was also increased connectivity in the HCAS group in the RUM condition between the R-precuneus and parts of the L-angular gyrus and supramarginal gyrus in comparison to the LCAS group; the opposite effect was observed in the ABS condition. The R-frontal pole showed decreased connectivity in the HCAS group in the RUM condition with four effect clusters in the right

TABLE 4 | Group differences in gPPI rumination induction functional connectivity.

Seed [*x y z*]	Effect [*x y z*]	Cluster size	Peak *Z*	*p*-value for cluster FDRc	HCAS		LCAS		Cohen's *d*
					RUM mean β	ABS mean β	RUM mean β	ABS mean β	
L-Precuneus [−4 −58 32]	L-Lateral occipital cortex, supramarginal gyrus [−30 −62 38]	114	3.91	0.014	0.11 (0.33)	−0.07 (0.35)	−0.08 (0.25)	0.15 (0.29)	1.43
	Bilateral precuneus [0 −66 22]	104	4.85	0.012	−0.11 (0.40)	0.14 (0.30)	0.08 (0.35)	−0.16 (0.31)	1.44
L-Precuneus [−8 −52 28]	L-Frontal pole [−42 58 −2]	168	4.46	0.001	0.24 (0.45)	−0.22 (0.53)	−0.29 (0.44)	−0.01 (0.43)	1.49
	R-Frontal pole [48 40 −6]	128	4.08	0.002	0.02 (0.29)	−0.21 (0.43)	−0.39 (0.41)	−0.06 (0.34)	1.55
L-Superior frontal gyrus [−2 56 38]	L-Superior parietal lobule, postcentral gyrus [−24 −38 56]	150	4.17	0.002	0.04 (0.25)	−0.21 (0.30)	−0.01 (0.28)	0.07 (0.30)	1.44
	R-Precuneus [8 −70 42]	114	4.50	0.012	−0.41 (0.44)	0.17 (0.76)	−0.25 (0.46)	−0.29 (0.54)	1.14
R-Precuneus [6 −52 26]	L-Angular gyrus, supramarginal gyrus [−42 −48 34]	86	4.46	0.041	0.05 (0.35)	−0.15 (0.18)	−0.22 (0.33)	0.03 (0.29)	1.31
R-Frontal pole [4 56 10]	R-Lingual gyrus [14 −56 0]	112	4.03	0.01	−0.20 (0.50)	−0.04 (0.32)	0.16 (0.42)	−0.14 (0.34)	1.22
	R-Planum temporale [58 −26 10]	111	4.07	0.01	−0.24 (0.38)	−0.12 (0.37)	0.09 (0.38)	0.24 (0.38)	1.22
	R-Postcentral gyrus [8 −42 62]	88	4.60	0.033	−0.26 (0.32)	−0.05 (0.37)	0.07 (0.34)	−0.17 (0.28)	1.28
	R-Heschl's gyrus, insular cortex [38 −22 8]	84	5.17	0.041	−0.19 (0.26)	−0.08 (0.26)	0.04 (0.22)	−0.23 (0.29)	1.56
R-Anterior cingulate cortex [5 28 18]	Bilateral precentral, R-postcentral gyri [4 −32 56]	96	4.34	0.022	−0.48 (0.66)	−0.20 (0.54)	0.24 (0.39)	−0.11 (0.43)	1.53
	R-Pre–postcentral gyri [14 −32 72]	90	4.25	0.030	−0.37 (0.39)	−0.18 (0.48)	0.28 (0.57)	−0.16 (0.49)	1.44

L, left hemisphere; R, right hemisphere; HCAS, high-CAS group; LCAS, low-CAS group; RUM, rumination condition in RumInd-M; ABS, abstract condition in RumInd-M.

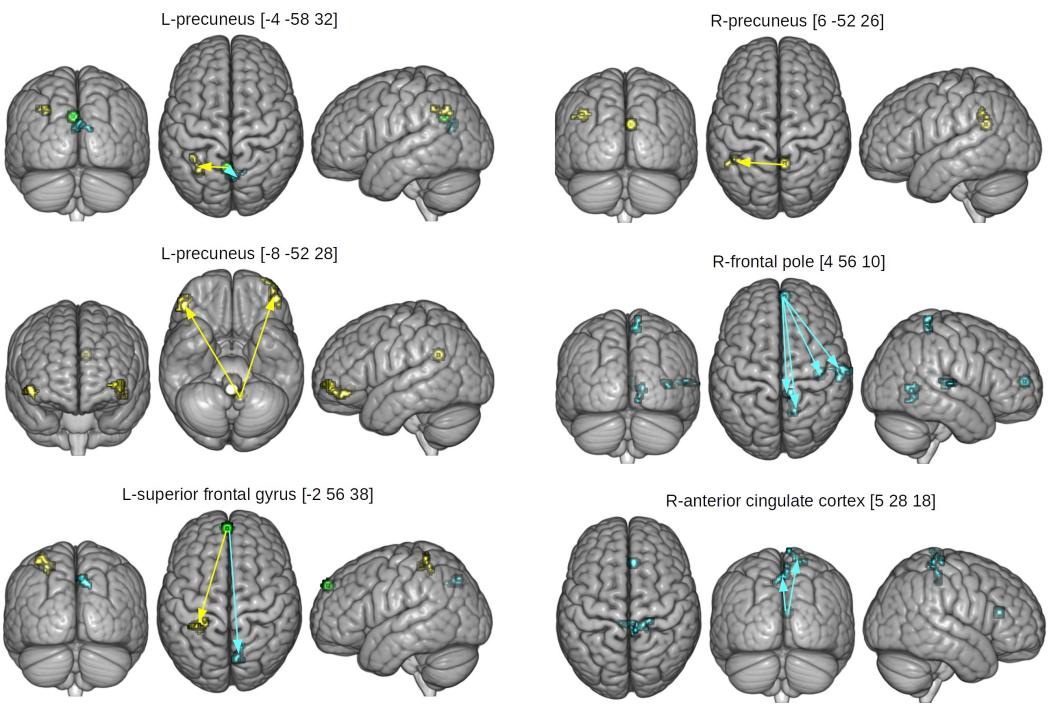

FIGURE 4 | Seed and effect clusters for gPPI analyses. Yellow clusters depict increased connectivity in the HCAS group in the RUM condition and/or decreased connectivity in the ABS condition in comparison to the LCAS group, cyan clusters depict decreased connectivity in the HCAS group in the RUM condition and/or increased connectivity in the ABS condition in comparison to the LCAS group. Green clusters depict seeds with bidirectional effects. Beginnings of arrows mark the seeds and ends mark the effects. For details of seeds, see **Table 4**.

temporal and right parietal lobes (see **Table 4** for details) in comparison to the LCAS group; opposite effects were observed in the ABS condition. A similar pattern of connectivity was observed in the R-anterior cingulate cortex and its effect clusters – bilateral precentral and R-postcentral gyri, and R-pre- and postcentral gyri. All presented interaction effects are significant with large effect sizes of Cohen's $d > 1$.

Resting State Functional Connectivity Results

The between-group differences in rsfMRI functional connectivity are presented in **Table 5** and **Figure 5**. The HCAS group showed increased connectivity in comparison to the LCAS group between the L-insula and the L-central opercular cortex and planum temporale. Similarly, stronger connectivity in the HCAS group was found for the seed in the R-dorsolateral prefrontal cortex leading to three resulting clusters in the R-occipital pole and intracalcarine cortex, R-occipital pole and lingual gyrus, and the L-intracalcarine cortex and lingual gyrus. On the other hand, there was decreased connectivity in the HCAS group in comparison to the LCAS group between the R-anterior cingulate cortex and the L-frontal pole. All differences were large in effect with all values of $d > 1$.

DISCUSSION

The present study used the rumination induction fMRI task and rsfMRI method to disentangle differences in the neural functioning of people with elevated levels of CAS in comparison to people with low levels of CAS. We ensured that the groups had extreme characteristics by pre-selecting two subsamples of people with low and high results on various measures of CAS and, additionally, by excluding participants with non-extreme and inconclusive results on the day of the study. A series of self-assessment questionnaires before, during, and after the fMRI procedure was used to address different levels of CAS, psychopathology symptoms, and negative emotions.

Group Differences in Self-Assessment

By their construction, the studied groups differed significantly on all used measures of CAS – the CAS-1 questionnaire, rumination, and metacognitive beliefs concerning the need to control thoughts as well as the perceived inability to control thoughts and the associated dangers. Nevertheless, both groups also differed in levels of psychopathology symptoms – both depressive (Papageorgiou and Wells, 2003, 2009; Fergus et al., 2012, 2013) and anxiety symptoms (Wells, 2005; Fergus et al., 2012, 2013), as well as pain symptoms. This result is in line with numerous studies on the relationships of psychopathology with somatic symptoms and complaints (Bair et al., 2003; Kroenke, 2003; Tsang et al., 2008). It is noteworthy that the groups did not differ in terms of physical illnesses and concerns reported in SCID-I (cf. Dragan and Kowalski, unpublished). The discrepancy between lack of difference in number of physical illnesses and concerns in SCID-I and large difference in self-reported levels of pain symptoms may be due to self-focused attention and threat monitoring in people with high levels of CAS, resulting in fixation of attention on bodily sensations that would otherwise go unnoticed. Such a mechanism would be consistent with an understanding of health anxiety based on the metacognitive model (Melli et al., 2018).

There were medium to large group differences in reported assessments of sadness and anxiety during rumination induction, but not in assessments of engagement. The HCAS group scored significantly higher on levels of these negative emotions not only when assessing their mood after the rumination condition but also, with smaller effect size, after reading the abstract sentences. Results from previous studies on patients with depression are mixed: in one study there were no differences in negative affect between MDD patients and controls during rumination induction despite initial differences (Berman et al., 2014), and another study (Burkhouse et al., 2017) found a significant effect of group, as remitted MDD adolescents had higher sadness ratings during both rumination and abstract conditions. Our study dealt with people with time-persistent high or low levels of CAS, so these results may indicate that CAS levels are a prominent characteristic related to experiencing negative affect during rumination induction. This could serve as an explanation of remitted MDD adolescents having higher negative affect scores at all times (Burkhouse et al., 2017) and current MDD patients (Berman et al., 2014) having such scores only initially, before rumination induction. This hypothesis needs to be verified by further studies which take these results about CAS levels into account. The large-effect group differences in levels of post-fMRI assessments of anxiety and negative emotions are also in line with this interpretation. Unfortunately, we did not collect pre-rumination-induction assessments of affect, which would enable the comparison of effects of group as well as group and time interactions.

Effects of Negative and Abstract Thinking

The results pertaining to main effects of conditions are partially in line with previous results about rumination induction (Cooney et al., 2010). The RUM > ABS direct comparison in our study revealed neural activations in the bilateral precunei, middle cingulate cortex, L-paracingulate gyrus, bilateral superior frontal gyri, and bilateral frontal poles. Cooney et al. (2010) reported a similar pattern of activations with larger parts of the frontal cortices as well as the occipital and temporal gyri, but using a lenient statistical threshold. This indicates engagement of the DMN (Greicius et al., 2003) with the most prominent activation in both precunei (Zhang and Chiang-shan, 2012). Precuneal activity is often linked to self-referential processing (Kjaer et al., 2002; Lou et al., 2004) and depressive rumination (Johnson et al., 2009; Cooney et al., 2010; Milazzo et al., 2014; Burkhouse et al., 2017). The medial parts of the prefrontal cortex are also associated with self focused attention (Gusnard et al., 2001) and emotional responses (Lane et al., 1997). Such a pattern

TABLE 5 | Group differences in resting state functional connectivity.

Seed [*x y z*]	Effect [*x y z*]	Cluster size	Peak *Z*	*p*-Value for cluster size FDRc	HCAS mean *Z*	LCAS mean *Z*	Cohen's *d* (CI 90%)
HCAS > LCAS							
L-Precuneus [−4 −58 32]	R-Lateral occipital cortex, fusiform gyrus [28 −86 −12]	140	4.37	0.002	0.02 (0.09)	−0.09 (0.13)	0.98 (0.52 – 1.45)
L-Precuneus [−8 −52 28]	R-Lateral occipital cortex [36 −84 −4]	71	3.85	0.043	0.06 (0.11)	−0.06 (0.14)	0.95 (0.49 – 1.41)
L-Insula [−41 −3 −14]	L-Central opercular cortex [−48 4 −2]	98	4.85	0.012	0.21 (0.09)	0.11 (0.06)	1.31 (0.82 – 1.79)
R-Dorsolateral prefrontal cortex [30 10 50]	L-Intracalcarine cortex, lingual gyrus [−8 −84 0]	100	4.31	0.010	0.05 (0.07)	−0.05 (0.11)	1.09 (0.62 – 1.55)
	R-Occipital pole, intracalcarine cortex [12 −90 6]	83	4.03	0.013	0.05 (0.07)	−0.04 (0.09)	1.12 (0.65 – 1.59)
	R-Occipital pole, lingual gyrus [6 −92 −6]	61	4.18	0.032	0.06 (0.09)	−0.05 (0.10)	1.16 (0.69 – 1.63)
LCAS > HCAS							
R-Anterior cingulate cortex [10 30 −4]	L-Frontal pole [−32 64 6]	84	4.21	0.023	0.01 (0.07)	0.10 (0.06)	−1.38 (−1.87 – −0.90)

L, left hemisphere; R, right hemisphere; HCAS, high-CAS group; LCAS, low-CAS group.

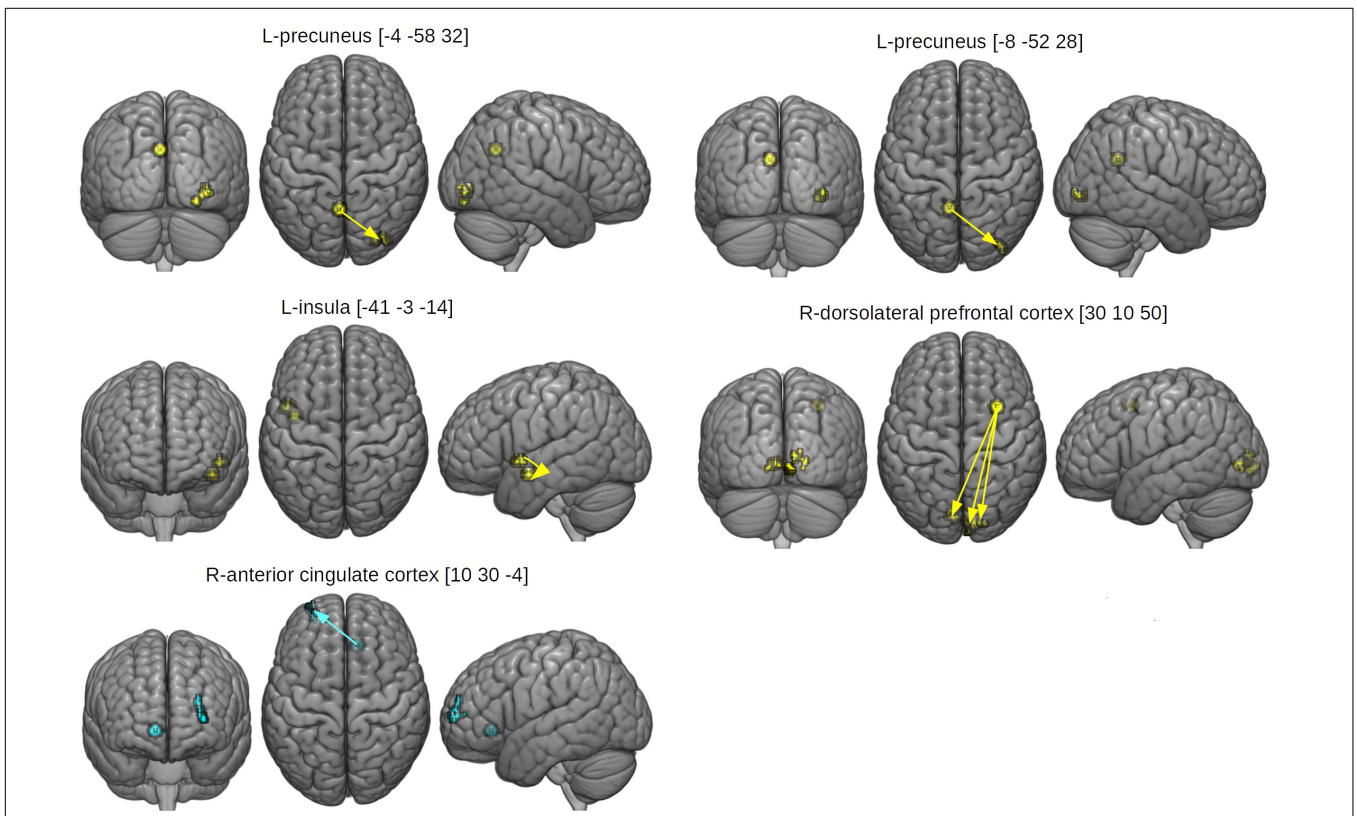

FIGURE 5 | Seed and effect clusters of rsfMRI analyses. Yellow clusters depict increased connectivity in the HCAS group in comparison to the LCAS group. Cyan clusters depict decreased connectivity in the HCAS group in comparison to the LCAS group. Beginnings of arrows mark the seeds and ends mark the effects. For details, see **Table 5**.

of activation during negative thinking induction may reflect cognitive components of negative thinking, specifically self-focused attention and self-referential processing. There were no significant brain activations in regions involved in emotional processing in the RUM > ABS comparison, i.e., in the amygdalae, parahippocampal gyri, or insulae.

Interestingly the ABS > RUM contrast (not reported by Cooney et al., 2010) revealed strong activations in the bilateral

middle temporal gyri, bilateral supramarginal gyri, L-precentral gyrus, R-middle and inferior frontal gyri, L-precentral gyrus and bilateral frontal poles. Widely distributed cortical activations in parts of the frontal poles (considered functionally as the dorsolateral prefrontal cortex) and parts of the parietal lobes can be identified as parts of the CEN (Corbetta and Shulman, 2002). The activity of the CEN, in opposition to the DMN, is associated with performing cognitive tasks, attention functioning, and working memory. The CEN as well as middle temporal regions and supplementary motor areas are also part of the "task-positive network" (Fox et al., 2005), which is a net of functionally correlated regions engaged in attention and working memory. This may indicate that abstract sentences engaged participants in tasks that required their attentional resources and were cognitively demanding.

The obtained patterns of neural activity specific to negative and abstract sentences are different and emphasize cognitive differences between these two types of thinking. It is also worth noting that both the DMN and CEN are engaged in the process of mind wandering (Christoff et al., 2009). In light of our results, this may indicate that mind wandering is comprised of self-referential rumination and dwelling on abstract cognitions.

Group Differences in Modified Rumination Induction

As rumination induction has scarcely been used to-date in fMRI studies, we based our hypotheses concerning group differences on results obtained by Cooney et al. (2010) in a group of depressed patients. We did not replicate these results, i.e., we did not uncover any significant group differences between HCAS and LCAS groups in rumination induction in the basic fMRI analysis. There may be several reasons for this. The first reason may be the very design of the rumination induction task: it is comprised of blocks of five sentences which each last 30 s and are divided by 10 s fixation crosses, which gives almost 200 s per block. This may subject the obtained data to physiological noise (Liu, 2016) or noise due to the instabilities of the magnetic field inside the scanner (Smith et al., 1999). As such, long blocks prevent the filtering of low-frequency changes in the fMRI signal. Thus, it would be recommended to use shorter blocks or event-related paradigms in future studies. The second reason may be that the sentences used in our study did not directly tap into the individual experiences of participants, but were more general, aiming to evoke rumination or worry in every person, regardless of their personal experiences. This may have resulted in weaker responses to the stimuli used. It may be expected that personalized ruminative sentences would evoke much higher responses in participants (cf. Berman et al., 2014; Burkhouse et al., 2017). Another reason may be the heterogeneity of obtained results, as high levels of CAS can manifest in different ways, with a person developing mood or anxiety disorders or comorbid disorders, producing differences on the cognitive level which could result in high variability of the fMRI signal across the whole brain. However, it is also possible that the results of Cooney et al. (2010) are not replicable. The authors used a rather liberal statistical threshold. Moreover they employed AFNI and AlphaSim software, in which a bug which elevates levels of false positive results has been identified (Eklund et al., 2016). Taking all the above into account, it is possible that in the rumination induction task used, brain activity related to repetitive negative thinking is similar in both sub-populations and potential between-group differences are not detectable with 'static' general linear model analysis. Thus we decided to seek possible between-group differences, delving into more dynamic temporal characteristics of brain activity, i.e., applying functional connectivity analyses.

Generalized Psychophysiological Interactions

The results of this study provide the first evidence that high levels of CAS are related to disrupted patterns of functional neural connectivity. Moreover, the between-group differences were found not only during rumination and worry, but also in abstract thinking. We conducted a gPPI functional connectivity analysis using areas found to be active in the RUM condition as seeds as well as ROIs based on meta-analytical literature on mood and anxiety disorders. The results show disrupted functional connectivity in the HCAS group within the DMN – the precunei, the medial parts of the prefrontal cortices, and parts of the occipital cortex (Greicius et al., 2003; Zhang and Chiang-shan, 2012) – during evoked negative thoughts. This may indicate a heightened tendency toward self-referential thinking and focusing attention on the self (Raichle et al., 2001; Buckner et al., 2008). A similar pattern of functional connectivity was also found in depression and interpreted as an inability of MDD patients to down-regulate cognitive activity broadly associated with the DMN (Sheline et al., 2009).

There was also an interaction indicating a pattern of heightened connectivity in the RUM condition and/or lowered connectivity in the ABS condition in the HCAS group in comparison to the LCAS group between the L-precuneus and bilateral ventrolateral prefrontal cortices (vlPFC), which play a role in emotion processing in MDD (Keedwell et al., 2005). Furthermore the vlPFC are associated with anxiety (in primates; Agustín-Pavón et al., 2012) and, more specifically, attention bias to both threatening and neutral stimuli in anxiety and anxiety related disorders (Sylvester et al., 2012) and PTSD (Fani et al., 2012). Previous research on adolescents (Guyer et al., 2008; Monk et al., 2008) has shown that functioning of the ventrolateral prefrontal cortex may be modulated by the amygdala in social phobia and GAD. Current results suggest that the functioning of the vlPFC is modulated by disrupted functioning of the DMN, particularly the precuneus, which may "override" the regulatory role of the vlPFC in emotional processing and indicates the proneness of HCAS subjects to attention bias in self-referential processing (Wells, 2009).

We also observed a disrupted connectivity pattern in parts of the DMN during the abstract condition in the HCAS group. Interaction indicating increased connectivity was found between medial parts of the frontal cortex and R-precuneus, as well as within frontal and parietal parts of the DMN, and also within the precunei. Diminished connectivity of the anterior part of the cingulate cortex, interpreted as part of the salience network (Peters et al., 2016), with medial parts of the somatosensory cortex was found in the HCAS group in both RUM and ABS conditions, as compared to the LCAS group. A similar pattern of connectivity was also found between part of the DMN – the medial part of the prefrontal cortex (mPFC) – and the medial part of the somatosensory cortex. The rostral part of the anterior cingulate cortex (ACC), which plays a role in the symptomatology of various emotional disorders (Etkin et al., 2006), was shown to modulate the activity of the amygdala in task (Etkin et al., 2006) and resting state (Margulies et al., 2007) fMRI. Diminished connectivity between the ACC, mPFC, and somatosensory cortex in the HCAS group may indicate the mechanism of disrupted regulation of perception of bodily sensations. This result may be in line with the higher scores on the pain and vegetative symptoms subscale of the SCL-27-plus in the HCAS group. Perhaps the disrupted connectivity of the ACC, mPFC, and somatosensory cortex is related to one of the core mechanisms of CAS – heightened vigilance and monitoring for threatening stimuli, including threatening bodily sensations, which is characteristic of anxiety and anxiety-related disorders (Wells and Carter, 2001; Esteve and Camacho, 2008; Ginzburg et al., 2014).

There was also an interaction indicating a decreased connectivity pattern in the RUM condition and/or increased connectivity pattern in the ABS condition in the HCAS group in comparison to the LCAS group between part of the mPFC, part of the DMN, and R-Heschl's gyrus, insular cortex, and R-planum temporale, which have been shown to be engaged in auditory (Storti et al., 2013) and language (Nakada et al., 2001; Buchsbaum et al., 2005) processing. These results are also consistent with diminished resting state connectivity in Heschl's gyrus and the planum temporale in high trait-anxiety participants (Modi et al., 2015). Taking into account that Heschl's gyrus is engaged in both task-elicited and spontaneous inner speech (Hurlburt et al., 2016), it may be hypothesized that the disrupted connectivity of the DMN, mPFC in this case, and parts of auditory and language circuitries reflects the tendency for repetitive negative thinking typical of HCAS participants (Wells, 2009).

These results may not only serve as evidence for difficulty in down-regulating DMN activity in HCAS subjects during ruminative and abstract thinking, but also suggest a more global pattern of functional connectivity during various types of thinking and diminished cognitive control (Peters et al., 2016). This conclusion is supported by higher amplitudes of changes in connectivity between conditions in the HCAS group in comparison to the control group (see beta values in **Table 3**). Different patterns of connectivity in the more cognitively demanding ABS condition between groups also suggests that high levels of CAS may be associated with disturbances in the performance of cognitive tasks observed in clinical groups (Austin et al., 2001; Bishop et al., 2004; Eysenck et al., 2007; Hammar and Årdal, 2009; Murrough et al., 2011), which is in line with the S-REF model and the metacognitive theory of psychological disorders (Wells and Matthews, 1994; Wells, 2009).

The described results are also in line with those showing connectivity disruptions in rsfMRI and task-based fMRI in MDD patients (Zhang et al., 2011; Sambataro et al., 2014; Palmer et al., 2015) and anxiety disorder patients (Ding et al., 2011; Lei et al., 2015). This suggests that clinical levels of psychopathology and clinical diagnoses may not be necessary to observe disrupted patterns of functional connectivity in the brain. High levels of CAS may serve as an underlying factor not only for the symptoms observed in various clinical afflictions, but also can be associated with corresponding patterns of neural functioning.

Resting State Functional Connectivity

In the current study, we also examined functional connectivity from brain activity recorded during a 10-min-long resting state fMRI procedure. We found the HCAS group to be characterized by stronger connectivity between several brain regions as compared to the LCAS group. First, the HCAS group showed stronger functional connectivity between the posterior part of the insula, a region involved, inter alia, in emotional processing during memory retrieval (Phan et al., 2002) and part of the opercular cortex in the left hemisphere, which is associated with auditory imagery (Lima et al., 2015). This pattern of connectivity could reflect the process of repetitive negative thinking occurring in the HCAS group – with interplay between parts of brain associated with emotion processing during memory retrieval (Phan et al., 2002) and verbal imagery. Increased connectivity was also found between the R-dorsolateral prefrontal cortex, which is associated with working memory and a part of the CEN (Corbetta and Shulman, 2002), and medial parts of the occipital lobe cortex associated with word recognition and processing (Mechelli et al., 2000) and visual processing (Kozlovskiy et al., 2014). Perhaps this increased connectivity may reflect common activations of these structures on a daily basis during the frequent rumination, worry, and reflection of the participants in the HCAS group. This is consistent with the results of the questionnaires they filled-in immediately before the fMRI study. It is noteworthy that diminished, not increased, connectivity was found between frontal and occipital brain regions in patients with social anxiety disorder (Ding et al., 2011). This result was interpreted by the authors as disrupted processing of visual stimuli in social contexts. Similarly, our results may suggest that CAS is an underlying factor of the heightened salience of threatening social cues in social anxiety disorder. This calls for investigation in further studies, as the results of this and other studies are mixed.

There was also a pattern of decreased connectivity found in the HCAS group as compared to the control group. This pattern was observed between part of the ACC and part of the ventral frontal pole which, again, are parts of the salience and CENs, respectively. Disruption in this connection was found in patients with GAD and interpreted as a dysfunction of top-down control over emotion regulation (Mochcovitch et al., 2014).

In general, the obtained results can be understood as altered interplay between different brain networks in people with high levels of CAS. Similar abnormalities were reported in studies on different clinical disorders such as depression (Zhang et al., 2011; Mulders et al., 2015; Peters et al., 2016) and social anxiety (Ding et al., 2011; Liu et al., 2015). This points to CAS as a probable factor underlying the clinical symptomatology and disrupted neural functional connectivity in people with different clinical afflictions, or even in people without a current diagnosis but with a high risk of developing emotional disorders.

CONCLUSION

To our knowledge, this is the first study to explore the neural correlates of CAS. In this study we showed that treatment- and diagnosis-naive people with high levels of CAS differ substantially from people with low levels of this syndrome on various psychopathology and affect measures. Nearly half of the HCAS group was diagnosed with at least one current psychiatric disorder, predominantly mood and anxiety disorders as well as PTSD. We also demonstrated a large difference in self-assessment in these groups during repeated induction of negative thinking. These serve as proof-of-concept results of the metacognitive theory of emotional disorders (Wells, 2009). Contrary to our first hypothesis, we had no success in replicating rumination induction results in depressed participants (Cooney et al., 2010), for which there may be methodological and theoretical reasons. Irrespective of previous results, we demonstrated that neuronal activity during negative thinking is strongly related to neural activation of the DMN and that brain activity patterns during abstract thinking resemble the CEN. We were able to demonstrate evidence for our two hypotheses regarding differences in functional connectivity between groups. We showed, that low- and high-CAS groups differed in measures of functional connectivity during rumination and worry as well as during abstract thinking and resting state fMRI: high levels of CAS were related to disrupted patterns of connectivity within and between various brain networks – the DMN, the salience network, and the CEN. Overall, our results suggest that people with high levels of CAS tend to have disrupted neural processing in the areas of self-referential, task-oriented, and emotional processing. The obtained results are broadly analogous to results obtained in fMRI studies of different clinical groups with mood, anxiety, and PTSDs, which serves as an argument for recognizing high levels of CAS as an underlying factor of emotional disorders and their neural correlates. These results are consistent with the theoretical underpinnings of the metacognitive theory of psychopathology, suggesting a common mechanism of emotional disorders originating in CAS and laying the foundations for further exploration of neural correlates of CAS. Future studies should use different, better-established fMRI paradigms and more differentiated groups, such as people with high levels of CAS with and without clinical diagnoses.

AUTHOR CONTRIBUTIONS

JK, MW, AM, and MD wrote the manuscript. JK and MD conducted the research. JK, MW, and AM analyzed the MRI data. MW and AM supervised the MRI part of the study. MD supervised the research and analyses.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyg.2019.00648/full#supplementary-material

REFERENCES

Agustín-Pavón, C., Braesicke, K., Shiba, Y., Santangelo, A. M., Mikheenko, Y., Cockroft, G., et al. (2012). Lesions of ventrolateral prefrontal or anterior orbitofrontal cortex in primates heighten negative emotion. *Biol. Psychiatry* 72, 266–272. doi: 10.1016/j.biopsych.2012.03.007

Austin, M. P., Mitchell, P., and Goodwin, G. M. (2001). Cognitive deficits in depression: possible implications for functional neuropathology. *Br. J. Psychiatry* 178, 200–206. doi: 10.1192/bjp.178.3.200

Bair, M. J., Robinson, R. L., Katon, W., and Kroenke, K. (2003). Depression and pain comorbidity: a literature review. *Arch. Int. Med.* 163, 2433–2445. doi: 10.1001/archinte.163.20.2433

Bennett, H., and Wells, A. (2010). Metacognition, memory disorganization and rumination in posttraumatic stress symptoms. *J. Anxiety Disord.* 24, 318–325. doi: 10.1016/j.janxdis.2010.01.004

Berman, M. G., Misic, B., Buschkuehl, M., Kross, E., Deldin, P. J., Peltier, S., et al. (2014). Does resting-state connectivity reflect depressive rumination? A tale of two analyses. *NeuroImage* 103, 267–279. doi: 10.1016/J.NEUROIMAGE.2014.09.027

Birn, R. M., Molloy, E. K., Patriat, R., Parker, T., Meier, T. B., Kirk, G. R., et al. (2013). The effect of scan length on the reliability of resting-state fMRI connectivity estimates. *NeuroImage* 83, 550–558. doi: 10.1016/j.neuroimage.2013.05.099

Bishop, S., Duncan, J., Brett, M., and Lawrence, A. D. (2004). Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. *Nat. Neurosci.* 7:184. doi: 10.1038/nn1173

Brzozowski, P., Watson, D., and Clark, L. (2010). *Skala Uczuæ Pozytywnych I Negatywnych SUPIN: Polska Adaptacja Skali PANAS Davida Watsona i Lee Ann Clark: Podrêcznik*. Warszawa: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.

Buchsbaum, B. R., Olsen, R. K., Koch, P. F., Kohn, P., Kippenhan, J. S., and Berman, K. F. (2005). Reading, hearing, and the planum temporale. *NeuroImage* 24, 444–454. doi: 10.1016/j.neuroimage.2004.08.025

Buckner, R. L., Andrews-Hanna, J. R., and Schacter, D. L. (2008). The brain's default network: anatomy, function, and relevance to disease. *Ann. N. Y. Acad. Sci.* 1124, 1–38. doi: 10.1196/annals.1440.011

Burkhouse, K. L., Jacobs, R. H., Peters, A. T., Ajilore, O., Watkins, E. R., and Langenecker, S. A. (2017). Neural correlates of rumination in adolescents with remitted major depressive disorder and healthy controls. *Cognit. Affect. Behav. Neurosci.* 17, 394–405. doi: 10.3758/s13415-016-0486-4

Central Statistical Office (2017). *Demographic Atlas of Poland [stat.gov.pl/en]*. Warsaw: Central Statistical Office.

Christoff, K., Gordon, A. M., Smallwood, J., Smith, R., and Schooler, J. W. (2009). Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. *Proc. Natl. Acad. Sci. U.S.A.* 106, 8719–8724. doi: 10.1073/pnas.0900234106

Cooney, R. E., Joormann, J., Eugène, F., Dennis, E. L., and Gotlib, I. H. (2010). Neural correlates of rumination in depression. *Cognit. Affect. Behav. Neurosci.* 10, 470–478. doi: 10.3758/CABN.10.4.470

Corbetta, M., and Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nat. Rev. Neurosci.* 3:201. doi: 10.1038/nrn755

Ding, J., Chen, H., Qiu, C., Liao, W., Warwick, J. M., Duan, X., et al. (2011). Disrupted functional connectivity in social anxiety disorder: a resting-state fMRI study. *Magn. Reson. Imag.* 29, 701–711. doi: 10.1016/j.mri.2011.02.013

Donaldson, C., Lam, D., and Mathews, A. (2007). Rumination and attention in major depression. *Behav. Res. Ther.* 45, 2664–2678. doi: 10.1016/j.brat.2007.07.002

Dragan, M., and Dragan, W. (2011). Psychometric properties of the Polish version of the metacognitions questionnaire-30. *Psych. Polska* 4, 545–553.

Eklund, A., Nichols, T. E., and Knutsson, H. (2016). Cluster failure: why fMRI inferences for spatial extent have inflated false-positive rates. *Proc. Natl. Acad. Sci. U.S.A.* 113, 7900–7905. doi: 10.1073/pnas.1602413113

Esteve, M. R., and Camacho, L. (2008). Anxiety sensitivity, body vigilance and fear of pain. *Behav. Res. Ther.* 46, 715–727. doi: 10.1016/j.brat.2008.02.012

Etkin, A., Egner, T., Peraza, D. M., Kandel, E. R., and Hirsch, J. (2006). Resolving emotional conflict: a role for the rostral anterior cingulate cortex in modulating activity in the amygdala. *Neuron* 51, 871–882. doi: 10.1016/j.neuron.2006.07.029

Eysenck, M. W., Derakshan, N., Santos, R., and Calvo, M. G. (2007). Anxiety and cognitive performance: attentional control theory. *Emotion* 7:336. doi: 10.1037/1528-3542.7.2.336

Fani, N., Jovanovic, T., Ely, T. D., Bradley, B., Gutman, D., Tone, E. B., et al. (2012). Neural correlates of attention bias to threat in post-traumatic stress disorder. *Biol. Psychol.* 90, 134–142. doi: 10.1016/j.biopsycho.2012.03.001

Fergus, T. A., Bardeen, J. R., and Orcutt, H. K. (2012). Attentional control moderates the relationship between activation of the cognitive attentional syndrome and symptoms of psychopathology. *Pers. Ind. Diff.* 53, 213–217. doi: 10.1016/J.PAID.2012.03.017

Fergus, T. A., Valentiner, D. P., McGrath, P. B., Gier-Lonsway, S., and Jencius, S. (2013). The cognitive attentional syndrome: examining relations with mood and anxiety symptoms and distinctiveness from psychological inflexibility in a clinical sample. *Psychiatry Res.* 210, 215–219. doi: 10.1016/J.PSYCHRES.2013.04.020

Fisher, P. L., and Wells, A. (2005). Experimental modification of beliefs in obsessive-compulsive disorder: a test of the metacognitive model. *Behav. Res. Ther.* 43, 821–829. doi: 10.1016/j.brat.2004.09.002

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., and Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc. Natl. Acad. Sci. U.S.A.* 102, 9673–9678. doi: 10.1073/pnas.0504136102

Ginzburg, K., Tsur, N., Barak-Nahum, A., and Defrin, R. (2014). Body awareness: differentiating between sensitivity to and monitoring of bodily signals. *J. Behav. Med.* 37, 564–575. doi: 10.1007/s10865-013-9514-9

Greicius, M. D., Krasnow, B., Reiss, A. L., and Menon, V. (2003). Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proc. Natl. Acad. Sci. U.S.A.* 100, 253–258. doi: 10.1073/pnas.0135058100

Gusnard, D. A., Akbudak, E., Shulman, G. L., and Raichle, M. E. (2001). Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc. Natl. Acad. Sci. U.S.A.* 98, 4259–4264. doi: 10.1073/pnas.071043098

Guyer, A. E., Lau, J. Y., McClure-Tone, E. B., Parrish, J., Shiffrin, N. D., Reynolds, R. C., et al. (2008). Amygdala and ventrolateral prefrontal cortex function during anticipated peer evaluation in pediatric social anxiety. *Arch. Gen. Psychiatry* 65, 1303–1312. doi: 10.1001/archpsyc.65.11.1303

Hamilton, J. P., Etkin, A., Furman, D. J., Lemus, M. G., Johnson, R. F., and Gotlib, I. H. (2012). Functional neuroimaging of major depressive disorder: a meta-analysis and new integration of baseline activation and neural response data. *Am. J. Psychiatry* 169, 693–703. doi: 10.1176/appi.ajp.2012.11071105

Hammar, Å., and Årdal, G. (2009). Cognitive functioning in major depression-a summary. *Front. Hum. Neurosci.* 3:26. doi: 10.3389/neuro.09.026.2009

Hardt, J. (2008). The symptom checklist-27-plus (SCL-27-plus): a modern conceptualization of a traditional screening instrument. *Psychol. Soc. Med.* 5:Doc08.

Hurlburt, R. T., Alderson-Day, B., Kühn, S., and Fernyhough, C. (2016). Exploring the ecological validity of thinking on demand: neural correlates of elicited vs. spontaneously occurring inner speech. *PLoS One* 11:e0147932. doi: 10.1371/journal.pone.0147932

Ipser, J. C., Singh, L., and Stein, D. J. (2013). Meta-analysis of functional brain imaging in specific phobia. *Psychiatry Clin. Neurosci.* 67, 311–322. doi: 10.1111/pcn.12055

Johnson, M. K., Nolen-Hoeksema, S., Mitchell, K. J., and Levin, Y. (2009). Medial cortex activity, self-reflection and depression. *Soc. Cognit. Affect. Neurosci.* 4, 313–327. doi: 10.1093/scan/nsp022

Keedwell, P. A., Andrew, C., Williams, S. C., Brammer, M. J., and Phillips, M. L. (2005). The neural correlates of anhedonia in major depressive disorder. *Biol. Psychiatry* 58, 843–853. doi: 10.1016/j.biopsych.2005.05.019

Kjaer, T. W., Nowak, M., and Lou, H. C. (2002). Reflective self-awareness and conscious states: PET evidence for a common midline parietofrontal core. *NeuroImage* 17, 1080–1086. doi: 10.1006/nimg.2002.1230

Kornacka, M., Buczny, J., and Layton, R. L. (2016). Assessing repetitive negative thinking using categorical and transdiagnostic approaches: a comparison and validation of three polish language adaptations of self-report questionnaires. *Front. Psychol.* 7:322. doi: 10.3389/fpsyg.2016.00322

Koster, E. H. W., De Lissnyder, E., Derakshan, N., and De Raedt, R. (2011). Understanding depressive rumination from a cognitive science perspective: the impaired disengagement hypothesis. *Clin. Psychol. Rev.* 31, 138–145. doi: 10.1016/J.CPR.2010.08.005

Kowalski, J., and Dragan, M. (2019). Cognitive-attentional syndrome — the psychometric properties of the CAS-1 and multi-measure CAS-based clinical diagnosis. *Compr. Psychiatry* 91, 13–21. doi: 10.1016/j.comppsych.2019.02.007

Kozlovskiy, S. A., Pyasik, M. M., Korotkova, A. V., Vartanov, A. V., Kiselnikov, A. A., and Glozman, J. M. (2014). Selective involvement of lingual gyrus in working memory and perception of different types of visual stimuli. *J. Int. Neuropsychol. Soc.* 20:43.

Kroenke, K. (2003). Patients presenting with somatic complaints: epidemiology, psychiatric co-morbidity and management. *Int. J. Methods Psychiatr. Res.* 12, 34–43. doi: 10.1002/mpr.140

Kuncewicz, D., Dragan, M., and Hardt, J. (2014). Validation of the Polish version of the symptom checklist-27-plus questionnaire. *Psychiatr. Polska* 48, 345–358.

Lane, R. D., Fink, G. R., Chau, P. M. L., and Dolan, R. J. (1997). Neural activation during selective attention to subjective emotional responses. *Neuroreport* 8, 3969–3972. doi: 10.1097/00001756-199712220-00024

Lei, D., Li, K., Li, L., Chen, F., Huang, X., Lui, S., et al. (2015). Disrupted functional brain connectome in patients with posttraumatic stress disorder. *Radiology* 276, 818–827. doi: 10.1148/radiol.15141700

Lima, C. F., Lavan, N., Evans, S., Agnew, Z., Halpern, A. R., Shanmugalingam, P., et al. (2015). Feel the noise: relating individual differences in auditory imagery to the structure and function of sensorimotor systems. *Cereb. Cortex* 25, 4638–4650. doi: 10.1093/cercor/bhv134

Liu, F., Guo, W., Fouche, J. P., Wang, Y., Wang, W., Ding, J., et al. (2015). Multivariate classification of social anxiety disorder using whole brain

functional connectivity. *Brain Struct. Funct.* 220, 101–115. doi: 10.1007/s00429-013-0641-4

Liu, T. T. (2016). Noise contributions to the fMRI signal: an overview. *NeuroImage* 143, 141–151. doi: 10.1016/j.neuroimage.2016.09.008

Lou, H. C., Luber, B., Crupain, M., Keenan, J. P., Nowak, M., Kjaer, T. W., et al. (2004). Parietal cortex and representation of the mental self. *Proc. Natl. Acad. Sci. U.S.A.* 101, 6827–6832. doi: 10.1073/pnas.0400049101

Margulies, D. S., Kelly, A. C., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., and Milham, M. P. (2007). Mapping the functional connectivity of anterior cingulate cortex. *Neuroimage* 37, 579–588. doi: 10.1016/j.neuroimage.2007.05.019

McLaren, D. G., Ries, M. L., Xu, G., and Johnson, S. C. (2012). A generalized form of context-dependent psychophysiological interactions (gPPI): a comparison to standard approaches. *NeuroImage* 61, 1277–1286. doi: 10.1016/j.neuroimage.2012.03.068

Mechelli, A., Humphreys, G. W., Mayall, K., Olson, A., and Price, C. J. (2000). Differential effects of word length and visual contrast in the fusiform and Lingual gyri during. *Proc. R. Soc. Lon. B Biol. Sci.* 267, 1909–1913. doi: 10.1098/rspb.2000.1229

Melli, G., Bailey, R., Carraresi, C., and Poli, A. (2018). Metacognitive beliefs as a predictor of health anxiety in a self-reporting Italian clinical sample. *Clin. Psychol. Psychother.* 25, 263–271. doi: 10.1002/cpp.2159

Milazzo, A. C., Ng, B., Jiang, H., Shirer, W., Varoquaux, G., Poline, J. B., et al. (2014). Identification of mood-relevant brain connections using a continuous, subject-driven rumination paradigm. *Cereb. Cortex* 26, 933–942. doi: 10.1093/cercor/bhu255

Mochcovitch, M. D., da Rocha, Freire, R. C., Garcia, R. F., and Nardi, A. E. (2014). A systematic review of fMRI studies in generalized anxiety disorder: evaluating its neural and cognitive basis. *J. Affect. Disord.* 167, 336–342. doi: 10.1016/j.jad.2014.06.041

Modi, S., Kumar, M., Kumar, P., and Khushu, S. (2015). Aberrant functional connectivity of resting state networks associated with trait anxiety. *Psychiatry Res. Neuroimage* 234, 25–34. doi: 10.1016/j.pscychresns.2015.07.006

Monk, C. S., Telzer, E. H., Mogg, K., Bradley, B. P., Mai, X., Louro, H. M., et al. (2008). Amygdala and ventrolateral prefrontal cortex activation to masked angry faces in children and adolescents with generalized anxiety disorder. *Arch. Gen. Psychiatry* 65, 568–576. doi: 10.1001/archpsyc.65.5.568

Mor, N., and Winquist, J. (2002). Self-focused attention and negative affect: a meta-analysis. *Psychol. Bull.* 128:638. doi: 10.1037/0033-2909.128.4.638

Mulders, P. C., van Eijndhoven, P. F., Schene, A. H., Beckmann, C. F., and Tendolkar, I. (2015). Resting-state functional connectivity in major depressive disorder: a review. *Neurosci. Biobehav. Rev.* 56, 330–344. doi: 10.1016/j.neubiorev.2015.07.014

Murrough, J. W., Iacoviello, B., Neumeister, A., Charney, D. S., and Iosifescu, D. V. (2011). Cognitive dysfunction in depression: neurocircuitry and new therapeutic strategies. *Neurobiol. Learn. Mem.* 96, 553–563. doi: 10.1016/j.nlm.2011.06.006

Myers, S. G., Fisher, P. L., and Wells, A. (2009a). An empirical test of the metacognitive model of obsessive-compulsive symptoms: fusion beliefs, beliefs about rituals, and stop signals. *J. Anxiety Disord.* 23, 436–442. doi: 10.1016/j.janxdis.2008.08.007

Myers, S. G., Fisher, P. L., and Wells, A. (2009b). Metacognition and cognition as predictors of obsessive-compulsive symptoms: a prospective study. *Int. J. Cognit. Ther.* 2, 132–142. doi: 10.1521/ijct.2009.2.2.132

Nakada, T., Fujii, Y., Yoneoka, Y., and Kwee, I. L. (2001). Planum temporale: where spoken and written language meet. *Eur. Neurol.* 46, 121–125. doi: 10.1159/000050784

Nolen-Hoeksema, S., and Morrow, J. (1993). Effects of rumination and distraction on naturally occurring depressed mood. *Emotion* 7, 561–570. doi: 10.1080/02699939308409206

Nolen-Hoeksema, S., Wisco, B. E., and Lyubomirsky, S. (2008). Rethinking rumination. *Perspect. Psychol. Sci.* 3, 400–424. doi: 10.1111/j.1745-6924.2008.00088.x

Olatunji, B. O., Naragon-Gainey, K., and Wolitzky-Taylor, K. B. (2013). Specificity of rumination in anxiety and depression: a multimodal meta-analysis. *Clin. Psychol. Sci. Pract.* 20, 225–257. doi: 10.1111/cpsp.12037

Palmer, S. M., Crewther, S. G., Carey, L. M., and Team, T. S. P. (2015). A Meta-analysis of changes in brain activity in clinical depression. *Front. Hum. Neurosci.* 8:1045. doi: 10.3389/fnhum.2014.01045

Papageorgiou, C., and Wells, A. (2001). Metacognitive beliefs about rumination in recurrent major depression. *Cognit. Behav. Pract.* 8, 160–164. doi: 10.1016/S1077-7229(01)80021-3

Papageorgiou, C., and Wells, A. (2003). An empirical test of a clinical metacognitive model of rumination and depression. *Cognit. Ther. Res.* 27, 261–273. doi: 10.1023/A:1023962332399

Papageorgiou, C., and Wells, A. (2009). A prospective test of the clinical metacognitive model of rumination and depression. *Int. J. Cognit. Ther.* 2, 123–131. doi: 10.1521/ijct.2009.2.2.123

Patriat, R., Molloy, E. K., Meier, T. B., Kirk, G. R., Nair, V. A., Meyerand, M. E., et al. (2013). The effect of resting condition on resting-state fMRI reliability and consistency: a comparison between resting with eyes open, closed, and fixated. *NeuroImage* 78, 463–473. doi: 10.1016/j.neuroimage.2013.04.013

Paulesu, E., Sambugaro, E., Torti, T., Danelli, L., Ferri, F., Scialfa, G., et al. (2010). Neural correlates of worry in generalized anxiety disorder and in normal controls: a functional MRI study. *Psychol. Med.* 40:117. doi: 10.1017/S0033291709005649

Peters, S. K., Dunlop, K., and Downar, J. (2016). Cortico-striatal-thalamic loop circuits of the salience network: a central pathway in psychiatric disease and treatment. *Front. Syst. Neurosci.* 10:104. doi: 10.3389/fnsys.2016.00104

Phan, K. L., Wager, T., Taylor, S. F., and Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *NeuroImage* 16, 331–348. doi: 10.1006/nimg.2002.1087

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., and Shulman, G. L. (2001). A default mode of brain function. *Proc. Natl. Acad. Sci. U.S.A.* 98, 676–682. doi: 10.1073/pnas.98.2.676

Sambataro, F., Wolf, N. D., Pennuto, M., Vasic, N., and Wolf, R. C. (2014). Revisiting default mode network function in major depression: evidence for disrupted subsystem connectivity. *Psychol. Med.* 44, 2041–2051. doi: 10.1017/S0033291713002596

Sarisoy, G., Pazvantoglu, O., Ozturan, D. D., Ay, N. D., Yilman, T., Mor, S., et al. (2014). Metacognitive beliefs in unipolar and bipolar depression: a comparative study. *Nordic J. Psychiatry* 68, 275–281. doi: 10.3109/08039488.2013.814710

Sheline, Y. I., Barch, D. M., Price, J. L., Rundle, M. M., Vaishnavi, S. N., Snyder, A. Z., et al. (2009). The default mode network and self-referential processes in depression. *Proc. Natl. Acad. Sci. U.S.A.* 106, 1942–1947. doi: 10.1073/pnas.0812686106

Simmons, A. N., and Matthews, S. C. (2012). Neural circuitry of PTSD with or without mild traumatic brain injury: a meta-analysis. *Neuropharmacology* 62, 598–606. doi: 10.1016/J.NEUROPHARM.2011.03.016

Smith, A. M., Lewis, B. K., Ruttimann, U. E., Frank, Q. Y., Sinnwell, T. M., Yang, Y., et al. (1999). Investigation of low frequency drift in fMRI signal. *NeuroImage* 9, 526–533. doi: 10.1006/nimg.1999.0435

Solem, S., Myers, S. G., Fisher, P. L., Vogel, P. A., and Wells, A. (2010). An empirical test of the metacognitive model of obsessive-compulsive symptoms: replication and extension. *J. Anxiety Disord.* 24, 79–86. doi: 10.1016/j.janxdis.2009.08.009

Spada, M. M., Mohiyeddini, C., and Wells, A. (2008). Measuring metacognitions associated with emotional distress: factor structure and predictive validity of the metacognitions questionnaire 30. *Pers. Ind. Diff.* 45, 238–242. doi: 10.1016/J.PAID.2008.04.005

Spielberger, C., Gorsuch, R., and Lushene, R. (1970). *State-Trait Anxiety Inventory (STAI). Psy.Gu.Se.* Available at: https://psy.gu.se/digitalAssets/1307/1307827_bib-2010.pdf#page=182

Spinhoven, P., Drost, J., van Hemert, B., and Penninx, B. W. (2015). Common rather than unique aspects of repetitive negative thinking are related to depressive and anxiety disorders and symptoms. *J. Anxiety Disord.* 33, 45–52. doi: 10.1016/j.janxdis.2015.05.001

Starcevic, V., Berle, D., Milicevic, D., Hannan, A., Lamplugh, C., and Eslick, G. D. (2007). Pathological worry, anxiety disorders and the impact of co-occurrence with depressive and other anxiety disorders. *J. Anxiety Disord.* 21, 1016–1027. doi: 10.1016/j.janxdis.2006.10.015

Storti, S. F., Formaggio, E., Nordio, R., Manganotti, P., Fiaschi, A., Bertoldo, A., et al. (2013). Automatic selection of resting-state networks with functional magnetic resonance imaging. *Front. Neurosci.* 7:72. doi: 10.3389/fnins.2013.00072

Sylvester, C. M., Corbetta, M., Raichle, M. E., Rodebaugh, T. L., Schlaggar, B. L., Sheline, Y. I., et al. (2012). Functional network dysfunction in anxiety and anxiety disorders. *Trends Neurosci.* 35, 527–535. doi: 10.1016/j.tins.2012.04.012

Treynor, W., Gonzalez, R., and Nolen-Hoeksema, S. (2003). Rumination reconsidered: a psychometric analysis. *Cognit. Ther. Res.* 27, 247–259. doi: 10.1023/A:1023910315561

Tsang, A., Von Korff, M., Lee, S., Alonso, J., Karam, E., Angermeyer, M. C., et al. (2008). Common chronic pain conditions in developed and developing countries: gender and age differences and comorbidity with depression-anxiety disorders. *J. Pain* 9, 883–891. doi: 10.1016/j.jpain.2008.05.005

Watson, D., Clark, L. A., and Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *J. Pers. Soc. Psychol.* 54, 1063–1070. doi: 10.1037/0022-3514.54.6.1063

Wells, A. (1999). A metacognitive model and therapy for generalized anxiety disorder. *Clin. Psychol. Psychother. Int. J. Theory Pract.* 6, 86–95. doi: 10.1002/(SICI)1099-0879(199905)6:2<86::AID-CPP189>3.0.CO;2-S

Wells, A. (2005). The metacognitive model of GAD: assessment of meta-worry and relationship with DSM-IV generalized anxiety disorder. *Cognit. Ther. Res.* 29, 107–121. doi: 10.1007/s10608-005-1652-0

Wells, A. (2007). Cognition about cognition: metacognitive therapy and change in generalized anxiety disorder and social phobia. *Cognit. Behav. Pract.* 14, 18–25. doi: 10.1016/j.cbpra.2006.01.005

Wells, A. (2009). *Metacognitive Therapy for Anxiety and Depression*. London: The Guilford Press.

Wells, A., and Carter, K. (2001). Further tests of a cognitive model of generalized anxiety disorder: metacognitions and worry in GAD, panic disorder, social phobia, depression, and nonpatients. *Behav. Ther.* 32, 85–102. doi: 10.1016/S0005-7894(01)80045-9

Wells, A., and Cartwright-Hatton, S. (2004). A short form of the metacognitions questionnaire: properties of the MCQ-30. *Behav. Res. Ther.* 42, 385–396. doi: 10.1016/S0005-7967(03)00147-5

Wells, A., and Matthews, G. (1994). *Attention and Emotion: A Clinical Perspective*. Mahwah, NJ: Lawrence Erlbaum Associates.

Wells, A., and Sembi, S. (2004). Metacognitive therapy for PTSD: a core treatment manual. *Cognit. Behav. Pract.* 11, 365–377. doi: 10.1016/S1077-7229(04)80053-1

Wrześniewski, K., Matusik, D., and Sosnowski, T. (2002). *Inwentarz Stanu i Cechy Lêku STAI: Polska Adaptacja STAI: Podrêcznik*. Warszawa: Pracownia Testów Psychologicznych Polskiego Towarzystwa Psychologicznego.

Zhang, J., Wang, J., Wu, Q., Kuang, W., Huang, X., He, Y., et al. (2011). Disrupted brain connectivity networks in drug-naive, first-episode major depressive disorder. *Biol. Psychiatry* 70, 334–342. doi: 10.1016/j.biopsych.2011.05.018

Zhang, S., and Chiang-shan, R. L. (2012). Functional connectivity mapping of the human precuneus by resting state fMRI. *NeuroImage* 59, 3548–3562. doi: 10.1016/j.neuroimage.2011.11.023

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